ABSTRACTS OF WORLD MEDICINE

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Pathology

EXPERIMENTAL PATHOLOGY

830. **Autoimages of Tissues and Organs on Photographic Films. A Preliminary Communication.** (Получение самоизображения тканей и органов на фотопленке (Предварительное сообщение))
N. N. BELAVINA. *Бюллетень Экспериментальной Биологии и Медицины* [*Byull. eksper. Biol. Med.*] **38**, 76–78, Oct., 1954. 4 figs., 1 ref.

In the experiments here reported from the Institute of Experimental Biology, Moscow, fresh, unfixed tissues were applied in complete darkness directly on to photographic films, immobilized in that position between two glass plates, and wrapped in black paper. These preparations were kept at a temperature of 2° to 6° C. for varying [unstated] periods of time, and after "exposure" were placed in cold water so that the tissues could be separated from the films without damaging the emulsion. The films were then developed and fixed in the usual manner. By the use of panchromatic films an "autoimage" of the tissues was obtained in shades which more or less corresponded to the original colours.

The author is satisfied that the images obtained were not due either to tissue radioactivity or to ultraviolet radiation. Direct contact between the tissue concerned and the photographic emulsion is essential for a clear image; even such thin and permeable membranes as "cellophane" film distorts the image. The author suggests that the image may be produced by some chemical action of tissue fluid. This process is therefore quite different from autoradiography. *A. Swan*

831. **Experimental Study of Measles in Monkeys.** (Экспериментальное изучение кори на обезьянах)
N. E. RYAZANTSEVA and E. V. SMIRNOVA. *Журнал Микробиологии, Эпидемиологии и Иммунодиологии* [*Zh. Mikrobiol.*] 11–15, No. 11, Nov., 1954.

In the authors' view, failure in the past to infect monkeys with the virus of measles by inoculation with the blood of human patients has been due in part to the use of blood taken during a time when no virus was present in the patients' circulation. At the Institute of Virusology of the Armenian S.S.R. they have developed a test, based on the agglutination of virus absorbed on to bacteria, which enables the presence or absence of measles virus in the circulation to be determined precisely. [No details of the test and no references are given.] According to this test the quantity of virus in the circulation increases up to the 7th or 8th day of the incubation period and then decreases somewhat; it begins to rise again about the 10th to 13th day and reaches a maximum at the end of the prodromal period and on the first day of the rash; after that it decreases rapidly and the virus disappears from the blood on the 3rd or 4th day after the rash has appeared.

It is claimed that measles can be transmitted with 100% success to *Macaca mulatta* monkeys 6 to 35 months old by simultaneous inoculation with blood and catarrhal secretions subcutaneously or into the conjunctiva and upper respiratory tract, or by intradermal inoculation with blood alone. In the monkey two waves of virusaemia occur 5 to 6 and 8 to 11 days after inoculation respectively, an increase in titre of measles antibodies beginning between the 14th and 21st days. Monkeys similarly inoculated with chorio-allantoic cultures of the virus develop no clinical signs of the disease, but are rendered immune to inoculation with material from patients. Measles virus freeze-dried at −20° C. loses its pathogenic and immunogenic properties for monkeys, whereas virus freeze-dried at −76° C. loses its pathogenicity, but retains its immunogenicity.

Antibodies developed as a result of injection during pregnancy are present in the blood of the offspring at birth in the same titre as in the mother's blood, remaining at that level for the first month and disappearing altogether within 4 months. If the infection takes place during the last few days of pregnancy the virus passes through the placenta and causes typical measles in the offspring during the first few days of life. *K. S. Zinnemann*

832. **Specificity of Antineoplastic Phenomenon Induced in Mice by Carcinogenic Agents**
M. POLLARD and R. H. BUSSELL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 186–190, May, 1954. 3 figs., 9 refs.

An antineoplastic factor which arises in the spleen of mice after injection with methylcholanthrene was previously described by the authors (*Proc. Soc. exp. Biol. (N.Y.)*, 1953, **83**, 671). The chemical and genetic specificity of this phenomenon has now been demonstrated in further experiments carried out at the University of Texas Medical Branch, Galveston, in which mice received subcutaneous injections of methylcholanthrene (MCA), 1 : 2 : 5 : 6-dibenzanthracene (DBA), or 3 : 4-benzpyrene (BP) dissolved in cooking fat; when tumours arose, additional groups of two different strains of mice received similar injections of the carcinogen and were

killed after 1 to 2 weeks. Tumour and spleen tissues were then minced and explants of these were placed on opposite sides of tubes prepared for tissue culture.

It was shown that explants from MCA-induced tumours grew with their homologous spleen, with spleen from mice recently inoculated with DBA or BP, or with spleen from the other strain of mice recently inoculated with MCA; they failed to grow in the presence of spleen from mice of the same strain treated with MCA for 1 to 2 weeks. Analogous results were found when tumours were induced by DBA or BP, the anti-neoplastic activity being present only in the spleen of mice given short treatment with the carcinogen which had induced the tumour, and only in the same strain of mice. The phenomenon was transient, and disappeared with the emergence of the tumour. The interpretation of this phenomenon on an immunological basis is discussed. *H. G. Crabtree*

833. A Microspectroscopic Study of Arterioles in Benign and Malignant Hypertension

P. O'B. MONTGOMERY and E. E. MUIRHEAD. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 1181–1189, Nov.–Dec., 1954. 7 figs., 7 refs.

The microspectroscopic absorption characteristics of normal human and canine arterioles, human and canine arterioles showing acute arteriolar necrosis, and human arterioles showing hyaline sclerosis were determined and compared by direct film densitometry.

The absorption curves of these normal and abnormal arterioles show complete absorption from 250 to 290 μ. From 290 to 350 μ the curves show incomplete absorption and are qualitatively similar. These data support the view that the acute arteriolar necrosis of the bilaterally nephrectomized dog, the acute arteriolar necrosis of human malignant hypertension, and the hyaline sclerosis of human benign hypertension have a common pathogenesis related to alterations of the smooth muscle of the arteriolar media.—[Authors' summary.]

834. Experimental Nephritis Due to Type Specific Streptococci. I. The Effect of a Single Exposure to Type 12 Streptococci. II. The Effect of Repeated Exposure to Type 12 Streptococci

R. W. REED and B. H. MATHESON. *Journal of Infectious Diseases* [*J. infect. Dis.*] **95**, 191–201, 202–212, Sept.–Oct., 1954. 15 figs., 28 refs.

After a brief review of the published evidence suggesting that acute glomerulonephritis is a non-suppurative complication of infection with Lancefield's Group-A haemolytic streptococci, particularly those of Type 12, the authors of these two papers from Dalhousie University Medical School, Halifax, Nova Scotia, describe experiments in which rabbits were subjected to single and repeated infections with these organisms.

In the first study three groups of rabbits were given respectively (1) an intravenous injection of the filtrate of a culture of Strain H8 of the streptococcus in Todd–Hewitt broth, (2) an intravenous injection of the broth after sterilization, and (3) a subcutaneous injection of 0·1 ml. of whole culture of Strain H8; a fourth untreated group acted as a control. Blood pressure was determined by the ear-capsule method of Reed and Kropp (*J. Lab. clin. Med.*, 1944, **29**, 214) and the urine was examined at regular intervals. The rabbits in Groups 1 and 3 developed hypertension in 10 and 17 days respectively after infection, the blood pressure rising to a maximum of 45 mm. Hg (normal 25 to 30 mm. Hg), and albumin and erythrocytes appeared in the urine on the 18th to 20th day. The animals were killed on the 35th day, when the kidneys showed numerous small haemorrhages, cellular degeneration confined to the first convoluted tubule, and dilatation of the glomerular capillaries; fluid was present in the peritoneal cavity. A diagnosis of lower nephron nephrosis was made. Rabbits in Groups 2 and 4 showed no pathological changes. Repetition of the experiment in two further series of animals gave similar results, but when rabbits were infected with strains of streptococci of Types 3, 10, 17, 18, or 35 only minimal changes, or none, were observed in the blood pressure and urine.

In the second study three groups of rabbits were infected as before, and then two of the groups were re-infected on the 56th day, one with whole culture and one with the filtrate; the third group was not reinfected. All 3 groups developed changes as in the first study, but partially recovered although hypertension recurred in all groups at the 8th week. Urinary changes in the re-infected animals were very severe. The kidneys again showed mainly the tubular damage associated with lower nephron nephrosis, glomerular changes being comparatively slight.

The authors speculate on the nature of the nephritogenic substance, which appears to be present only in haemolytic streptococci of Type 12, and incline to the theory that it is a hapten and a non-protein. Further studies to elucidate the chemical nature of this substance are in progress. *G. Loewi*

835. Effects of Heparin on Experimental Nephritis in Rabbits

J. KLEINERMAN. *Laboratory Investigation* [*Lab. Invest.*] 3, 495–508, Nov.–Dec., 1954. 8 figs., 15 refs.

CHEMICAL PATHOLOGY

836. A Quick and Simple Method for Blood-sugar Estimation

J. LEE. *British Medical Journal* [*Brit. med. J.*] **2**, 1087–1088, Nov. 6, 1954. 1 fig., 5 refs.

A quick and simple method of estimating the blood sugar level is described in this paper from Charing Cross Hospital Medical School, London. The method is a modification of that of Sumner, in which use was made of the fact that there is a change in colour when the sugar in deproteinized blood filtrate is heated with dinitrosalicylic acid in alkaline solution. The modifications introduced consist in the use of smaller quantities of serum (0·2 ml.) and of the dinitrosaliyclic acid itself to precipitate the proteins. A set of permanent artificial colour standards for matching was also introduced.

The blood sugar content of 200 specimens to which glucose had been added to give levels in the range 80 to 560 mg. per 100 ml. was determined. It was found that with levels higher than 360 mg. per 100 ml. it was necessary to dilute the coloured solution in order to match it satisfactorily with the standard. With glucose solutions accurate results were obtained over the range 60 to 1,400 mg. per 100 ml. The colour was stable at least 30 minutes at room temperature, and immediate and delayed readings did not differ by more than 5%. A comparison of the findings by this method and those obtained by the method of Hagedorn and Jensen at levels between 90 mg. and 600 mg. per 100 ml. showed good correlation.

Details are given of the technique whereby the colour developed is compared visually with the standards. The blood sugar level in 204 diabetics was estimated by this method and by that of Folin and Wu, a good correlation between the results of the two methods being observed. In the range 60 to 150 mg. per 100 ml., the error in 65 out of 70 results did not exceed 20 mg., and in the range 150 to 350 mg. per 100 ml. the error in 125 out of 134 results did not exceed 30 mg.

It is suggested that this technique, which takes only 10 minutes to complete, affords a quick and reliable method of estimating the blood-sugar level with sufficient accuracy to be of value in an emergency, as a ward test, and in the management of diabetes in general practice.

R. F. Jennison

837. **Abnormal Glucose-tolerance Tests in Patients Treated with Sedative Drugs**

W. H. H. MERIVALE and R. A. HUNTER. *Lancet* [*Lancet*] 2, 939–942, Nov. 6, 1954. 1 fig., 9 refs.

At Guy's Hospital, London, the authors studied the results of oral glucose tolerance tests on 23 healthy adults and 16 patients receiving large doses of sedative drugs. The sedatives were mainly barbiturates, 3 of the patients undergoing continuous narcosis and 9 being established barbiturate addicts. The dosage of the barbiturates, most of which were medium- to short-acting ones, varied from 1½ gr. to 32 gr. [0·1 to 2·13 g.] daily. Some of the patients were also receiving chloral hydrate, codeine, paraldehyde, chlorpromazine, promethazine, or morphine. After the patient had taken by mouth 50 g. of glucose in 180 ml. of water, the true blood sugar level was determined on capillary specimens at half-hour intervals for 5 hours. In the healthy subjects the half-hourly determinations continued for only 2½ hours. In 7 patients the tests were carried out during heavy barbiturate medication and then repeated when the dosage was reduced or when the drug was withdrawn.

When the patients' blood sugar curves for the first 2½ hours were compared with the normal range as represented by those of healthy subjects, it was found that the former fell into 4 groups: (1) lag curve (4 cases), (2) prolonged hyperglycaemic curve (7); (3) hypoglycaemic curve (7); and (4) bizarre curve (5). The authors suggest that some of the lag curves and hyperglycaemic responses could be explained on the basis of inhibition by the barbiturate of the enzyme systems mediating the oxidation of glucose by the brain, heart, and liver, but that endocrine factors and an accelerated intestinal absorption of glucose could not be excluded. The hypoglycaemic curves are considered to be of interest in the light of the suggestion by other workers that barbiturate intoxication should be borne in mind in the differential diagnosis of islet-cell adenoma of the pancreas. However, the authors are unable to explain either these curves or the bizarre responses, but suggest that barbiturate medication should be considered as a possible cause of abnormality in the results of the glucose tolerance test, and that caution should be exercised in determining the insulin dosage of diabetics receiving barbiturates.

M. J. H. Smith

838. **Rapid Estimation of the Serum Vitamin B_{12} Level by a Microbiological Method**

R. H. GIRDWOOD. *British Medical Journal* [*Brit. med. J.*] 2, 954–956, Oct. 23, 1954. 9 refs.

The author describes a rapid method of estimating the level of vitamin B_{12} (cyanocobalamin) in the serum, using *Lactobacillus leichmannii* as the test organism. On comparison in a number of cases of the results obtained by this method with those obtained with *Euglena gracilis* as the test organism agreement was not always close, but the values were of the same order. The method described has the advantage of speed, giving an answer within 24 hours, and the author considers that, together with his differential urinary folic acid excretion test (*Lancet*, 1953, 2, 53; *Abstracts of World Medicine*, 1954, 15, 302), it is of value in the investigation of the pathogenesis of complex cases of megaloblastic anaemia.

The serum level of vitamin B_{12} was less than 130 $\mu\mu$g. per ml. in 34 out of 36 cases of pernicious anaemia in relapse, whereas it was below that level in only 2 out of 24 patients with other forms of megaloblastic anaemia (one with megaloblastic anaemia after partial gastrectomy and one with idiopathic steatorrhoea) and in only 3 of 50 control subjects, 2 of whom had macrocytic anaemia with a normoblastic marrow and responded to treatment with vitamin B_{12}.

Janet Vaughan

839. **The Value of Paper Electrophoresis of Serum Proteins in Diagnosis of Ascites**

H. E. M. KAY. *British Medical Journal* [*Brit. med. J.*] 2, 1025–1028, Oct. 30, 1954. 3 figs., 12 refs.

The author suggests that although there has been a tendency to overrate the value of paper electrophoresis of the serum proteins as a diagnostic aid, the method is still of considerable help for example, in differentiating conditions in which ascites is the main manifestation of disease.

In 38 cases of ascites (excluding that due to cardiac failure) seen at St. Thomas's Hospital, London, the total serum protein content was determined by the micro-Kjeldahl method and the serum protein fractions by paper electrophoresis. In 15 cases of carcinomatosis peritonei the mean α-2-globulin value was $1{\cdot}10 \pm 0{\cdot}25$ g. per 100 ml. and the γ-globulin value $1{\cdot}14 \pm 0{\cdot}53$ g. per 100 ml. The corresponding mean values in 16 cases of cirrhosis of the liver were $0{\cdot}50 \pm 0{\cdot}15$ g. and $2{\cdot}65 \pm 1{\cdot}13$ g. per 100 ml. respectively. The total protein, albumin,

α-1-globulin, and β-globulin values were about the same in the two groups. There was no characteristic pattern of the protein fractions in the remaining cases, which included 3 cases of pericarditis, 1 of subacute nephritis, and 3 miscellaneous cases. The author concludes that by examination of the distribution of serum protein fractions on the electrophoresis strips a clear distinction can be made between ascites due to malignant peritoneal metastases and that due to intrahepatic causes. Several of the cases in which a doubtful diagnosis was clarified by the results of electrophoresis are discussed in detail.

M. Lubran

840. **The Estimation of Serum Lipoproteins. A Micromethod Based on Zone Electrophoresis and Cholesterol Estimations**

G. S. Boyd. *Biochemical Journal* [*Biochem. J.*] **58**, 680–685, 1954. 5 figs., 20 refs.

HAEMATOLOGY

841. **Blood Coagulation and the L. E. Cell Phenomenon**

S. L. Lee, L. I. Schwartz, and S. Pariser. *Blood* [*Blood*] **9**, 965–970, Oct., 1954. 19 refs.

Having found that in blood rendered incoagulable by an anticoagulant there is a striking reduction in the intensity of the L.E.-cell phenomenon as compared with blood permitted to clot spontaneously in glass tubes, the authors, at the Mount Sinai Hospital, New York, attempted to determine the specific component of the coagulation process which is necessary for the activity of the L.E.-cell factor. Experiments showed that labile factor, S.P.C.A., thrombin, and fibrin played no part in this activation, but that a constituent released from platelets was necessary, the activity of which was proportional to the concentration of the platelets. When rabbit-brain thromboplastin was substituted for platelets in each experiment comparable results were obtained, suggesting that the thromboplastic factor might possibly be the significant fraction.

E. G. Rees

842. **Hemoglobin E, a Hereditary Abnormality of Human Hemoglobin**

A. I. Chernoff, V. Minnich, and S. Chong-Chareonsuk. *Science* [*Science*] **120**, 605–606, Oct. 15, 1954. 1 fig., 9 refs.

The authors report, from the University of Medical Sciences, Bangkok, the detection in 8 natives of Thailand of an abnormal haemoglobin which possessed the same electrophoretic mobility as the haemoglobin E discovered about the same time by Itano *et al.* (*J. Amer. chem. Soc.*, 1954, **76**, 2278) in the U.S.A. It is presumed that the two pigments are identical. Of the Thai subjects, 5 had clinical and haematological manifestations of Mediterranean (Cooley's) anaemia and were found to possess haemoglobins E and F; it is suggested the condition might properly be termed Mediterranean–haemoglobin-E disease. The other 3 patients, who were asymptomatic and whose blood contained haemoglobins E and A, were regarded as having the haemoglobin-E trait.

In the investigations made by filter-paper electrophoresis 10 specimens of haemoglobin were run simultaneously, using strips of Whatman 3MM paper 7·5 inches (19 cm.) wide which had been treated with a veronal buffer of *p*H 8·8 and ionic strength 0·06 and clamped between siliconized glass to prevent puddling. From 0·003 to 0·005 ml. of each of the haemoglobin solutions (6 to 12 g. per 100 ml.) was applied at the centre line, and runs of 10 to 14 hours were made at 350 volts and 14 to 16 mA. After the paper had been dried the migration spots could be seen without staining. Under these conditions the haemoglobins were in the following order of rate of migration: A, F, S, E, and C, haemoglobin E occupying an intermediate position between S and C. When haemoglobin E was eluted from the strip, dialysed, and analysed spectrophotometrically no deviation from normal adult haemoglobin could be detected in the absorption spectrum.

A detailed study of the family of one of the patients showed that haemoglobin E is genetically transmitted in a manner similar to other haemoglobins. Taking the intensity of electrophoretic spots as a quantitative guide, the authors suggest that haemoglobin E forms the major component in Mediterranean–haemoglobin-E disease and the minor component in the haemoglobin-E trait.

[Electrophoretic mobility may not always be the sole valid guide to the identity of different haemoglobin samples—compare, for example, haemoglobins D and S. As the number of known haemoglobins increases it becomes of special importance to run a battery of controls with every test; for this purpose the wide strip used by the authors is particularly suitable.] *A. J. Duggan*

843. **Studies of Different Methods of Determining the Leucocyte Sedimentation Rate and Its Relation to Nuclear Changes.** (Untersuchungen über verschiedene Methoden der Leukocytensenkung und ihre Beziehungen zur Kernverschiebung)

H. Schaper. *Folia haematologica* [*Folia haemat.* (*Lpz.*)] **72**, 201–228, 1954. 5 figs., 20 refs.

The leucocyte sedimentation rate was measured by the method of Schilling and Schulz, and the rate and strength of leucocyte agglomeration by the method of Tischendorf and Fritze, in samples of blood from 17 normal subjects. There was complete correlation between the time and strength of leucocyte agglomeration and the leucocyte sedimentation rate, whereas there was no correlation between these measurements and the erythrocyte sedimentation rate. Out of 18 cases of infectious diseases such as pulmonary tuberculosis, lung abscess, bronchitis, and pneumonia, the leucocyte sedimentation rate was increased in 17. Here, too, there was no correlation with the erythrocyte sedimentation rate, but there was a parallelism between the changes in the neutrophil nuclear index during the course of the infectious process and the changes in the leucocyte sedimentation rate and agglomeration time.

Leucocytes from a subject with normal leucocyte sedimentation rate clumped rapidly when added to the plasma of a patient with a raised leucocyte sedimentation rate, both subjects being of the same blood group. The

converse experiment resulted in no clumping, suggesting that a plasma factor is involved in the agglomeration of leucocytes which, the author suggests, is probably an opsonin-like substance. However, when leucocytes and plasma from healthy subjects of Groups A and B were intermixed, clumping occurred; this phenomenon is as yet unexplained. *M. Lubran*

844. **Detection of an Additional Rhesus Antibody by Absorption of Anti-A and Anti-B Agglutinins.** [In English]
I. DUNSFORD and P. NEWSTEAD. *Vox sanguinis* [*Vox Sanguinis* (*Amst.*)] **4**, 171–172, Nov., 1954. 1 ref.

MORBID ANATOMY AND CYTOLOGY

845. **The Histology and Histochemistry of Gargoylism**
I. M. P. DAWSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 587–604, 1954. 9 figs., 32 refs.

The author describes investigations carried out post mortem in the Department of Pathology of the University of Leeds in 4 cases of gargoylism in children aged 5 to 9.

The main macroscopic features were enlargement of the skull and brain, kyphosis, hepatosplenomegaly, thickening of the mitral valve, and coronary occlusion due to intimal thickening. Histologically, the central nervous system showed infiltration of neurones by granular or vacuolar material and loss of Nissl substance. In the liver there was extensive vacuolization of cells and disturbance of the architecture, while vacuolated cells were also present in the pulp and lining the sinusoids of the spleen. The thickening of the coronary intima and mitral valve was due to the presence of fibrous tissue containing large vacuolated cells. In 2 cases the bones showed arrest of epiphyseal growth, and in one of these vacuolated cells were seen in the periosteum and fibrocartilage.

In the central nervous system the infiltrate was present in formalin-fixed frozen sections and in paraffin sections, but was soluble in hot chloroform–methanol. It contained lipids (staining with Sudan black), which were probably acidic (staining blue with Nile blue) and unsaturated (giving a positive performic-acid–Schiff stain). Positive staining also occurred with the periodic-acid–Schiff method; this could have been due to the presence of either carbohydrate or lipid. In one case Baker's acid haematin stain for phosphatides gave a positive result. In only one case was it still present in frozen sections after formalin fixation; it was then stainable with Sudan IV, Sudan black, and by the periodic-acid–Schiff method. In another case it was similarly stainable in unfixed frozen sections, and also, after formol–calcium fixation, by Baker's method for phosphatides.

While the staining reactions of the neuronal infiltrate and of the infiltrate elsewhere were consistent with the material being a phosphatide or a cerebroside, the ready solubility, in aqueous fixatives, of the infiltrate in cells outside the nervous system suggested the presence of a polysaccharide element. The author therefore suggests that "the primary disturbance in gargoylism is one of polysaccharide or mucopolysaccharide metabolism, and that combination between polysaccharides and phosphatides or cerebrosides may occur in neurones and other tissues, producing substances of varying solubility."
M. C. Berenbaum

846. **Bone Tumours. A Histological Method of Classification**
R. T. WARWICK and A. D. THOMSON. *Archives of the Middlesex Hospital* [*Arch. Middx Hosp.*] **4**, 219–230, Oct., 1954. 11 figs., 7 refs.

The nomenclature and classification of bone tumours, which has hitherto been confused and complicated, can be simplified by the avoidance of such terms as "osteogenic" and by carrying subdivision only so far as is justified by the contrasting behaviour of the resulting groups. The present paper from the Bland-Sutton Institute of Pathology, Middlesex Hospital, London, offers a purely histological scheme of classification for primary malignant bone tumours, excluding those—such as Ewing's tumour and the malignant reticuloses—which arise from haematopoietic and other non-skeletal tissues in bone. The scheme is based on that proposed by Scarff (*Proc. roy. Soc. Med.*, 1937, **30**, 24), and groups the primary malignant skeletal tumours as follows. (1) Osteosarcoma. (2) Chondrosarcoma. (3) Fibrosarcoma. (4) Spindle-cell sarcoma. (5) Giant-cell tumour.

The term "osteoblast sarcoma" is put forward as a possible alternative to "osteosarcoma", the diagnostic feature of this type of lesion being the presence of irregular spicules of osteoid tissue formed and surrounded by malignant osteoblastic tumour cells showing marked cellular variation and pleomorphism.

The authors regard their 5 groups as distinct and report that they had no difficulty in classifying on this basis the majority of 180 primary malignant skeletal tumours seen at the hospital since 1925. They note, however, that occasional tumours of the osteosarcoma group contain variable amounts of cartilaginous tissue. The survival of patients in this series with each type of tumour is shown graphically. While the tumours of Group 1 are all highly malignant, the authors point out that there is considerable variation in the degree of malignancy of tumours in Groups 2, 4, and 5. In Groups 2 and 5 it is considered that histological assessment of the degree of malignancy of an individual tumour is feasible.
H. A. Sissons

847. **Cicatricial Cancer of the Lung in Relation to the Pathogenesis of Peripheral Carcinoma.** (Die Narbenkrebse der Lungen als Beitrag zur Pathogenese des peripheren Lungencarcinoms)
C. J. LÜDERS and K. G. THEMEL. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **325**, 499–551, 1954. 18 figs., bibliography.

This paper from the Wenckebach Hospital, Tempelhof, Berlin, follows up the earlier work of Rössle on the frequency of scars in relation to carcinoma of the lung. In a series of 2,000 necropsies performed in a 4-year period there were 74 cases of pulmonary carcinoma, and of these 21 were *Narbenkrebse*—that is, they possessed a

central scar which was believed to be related to the origin of the tumour. The tumours were nearly all peripheral, and nearly all peripheral tumours of the lung were of this type. Histologically, these tumours resembled those arising centrally, and such peculiarities as were found in the pattern of their metastases could probably be related to their peripheral site. The scars were chiefly tuberculous, but some were thought to be old infarcts.

[This paper is curiously complementary to that of Spencer and Raeburn (*J. Path. Bact.*, 1954, **67**, 187), who searched scars in the lung and found what they believed to be early carcinomata. Their criteria for the diagnosis of carcinoma have been criticized, whereas in the cases reported in this paper the tumours were undoubtedly carcinomata, the scars less certain. Yet to some extent the two studies reinforce each other.] *B. Lennox*

848. **Chronic Tuberculous Pneumonia.** (Pneumonies chroniques tuberculeuses)
—. MAGNIN and —. FÉROLDI. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 756–771, 1954. 11 figs.

The authors give details of the anatomical and histological findings in 30 specimens of lung tissue removed at operation at the Hauteville Sanatorium (University of Lyons) in cases of pulmonary tuberculosis in which radiography showed a localized opaque lesion. They believe that the condition found in these cases is different from those commonly causing such opacities, and refer to it as "chronic tuberculous pneumonia". Histologically, the lesion may consist of zones of pneumonia, encapsulated caseous foci, and areas of atelectasis and bronchial obstruction, so that the use of the term "pneumonia" may be misleading. It is considered that the diagnosis of this lesion is important from the therapeutic point of view, as when it is present collapse therapy is usually ineffective and may be harmful.
G. J. Cunningham

849. **The Liver in Ulcerative Colitis**
R. G. F. PARKER and E. J. C. KENDALL. *British Medical Journal* [*Brit. med. J.*] **2**, 1030–1032, Oct. 30, 1954. 13 refs.

In view of the differences of opinion regarding the frequency and significance of changes in the liver, particularly cirrhosis, as a result of ulcerative colitis, the authors have reviewed the post-mortem findings in the liver in all cases of ulcerative colitis, 73 in number, coming to necropsy at the Bernhard Baron Institute of Pathology of the London Hospital during the period 1914–53. Histological preparations of the liver had been made in 39 cases, and of these, fatty change was absent in 8, mild in 17, moderate in 5, and severe in 9 cases. None of the cases showed diffuse inflammatory-cell infiltration of the portal and periportal tissues, but 6 cases showed excess cellular infiltration (affecting, however, only a few portal tracts). Only one case of the 39 showed significant fibrosis; this patient also had a carcinoma of the extrahepatic bile ducts. Slight fibrous thickening of occasional portal tracts occurred in 4 cases, but there was no disruption of the lobular pattern of the liver. Cirrhosis had not been observed macroscopically in any of the 73 cases. Other lesions present were focal or irregularly distributed centrilobular necrosis in 5 cases, severe amyloidosis in 1 case, and carcinoma of the colon in 2 cases. No detailed studies of liver function had been made and clinical evidence of hepatic involvement was scanty. In no case had jaundice or splenomegaly been reported, and no clinical factors predisposing to the lesion were found, apart from recent pregnancy in 3 cases.

The authors conclude that there is no greater liability to the development of cirrhosis of the liver in patients with ulcerative colitis than in the population as a whole.
M. Lubran

850. **A Biopsy Study of the Kidney in Diabetes Mellitus**
H. P. TAFT, E. S. FINCKH, and R. A. JOSKE. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 189–201, Aug., 1954. 6 figs., bibliography.

At the Walter and Eliza Hall Institute and Royal Melbourne Hospital the authors performed biopsy of the right kidney under local analgesia, using a Franseen needle, after intravenous or retrograde pyelography in 20 cases of diabetes of varying severity in patients aged from 14 to 71 years. There was no haematuria or other complication. The specimens of renal tissue removed contained between 3 and 33 glomeruli (average 16).

Histological examination showed that the main glomerular changes, some of which are illustrated in photomicrographs, were: (1) diffuse increase of intercapillary acidophil material (11 cases); (2) "exudative" lesions, that is, masses of hyaline material replacing part of a capillary tuft or attached to the capsule (5 cases); (3) fibrosis resembling that caused by ischaemia (10 cases); and (4) nodular intercapillary masses (4 cases). Only the last finding is considered to be almost pathognomonic of diabetes. The intercapillary exudative and nodular material was positive to periodic-acid–Schiff staining and was thought to be probably a glycoprotein. In 14 cases the juxtaglomerular arterioles showed hyaline thickening, while in 7 the tubules contained hyaline or granular casts. The renal pathological changes were severe in 5 cases, minimal in 6, and absent in 9; they were, on the whole, more severe in patients with long-standing diabetes, and only in these were the nodular lesions seen. The predominance of renal lesions in women, reported by other workers, was confirmed in the present series, gross changes being present in biopsy specimens from 4 of 11 female patients, but in only 1 of 9 from males.

In a comparison with the clinical findings the histological changes were found to show close correlation with the presence of a systolic blood pressure of over 140 mm. Hg, retinopathy, systemic vascular disease, and proteinuria (but not of pyuria). No correlation, however, was found between the severity of renal change and the degree of control of hyperglycaemia and glycosuria. The correlation of biopsy findings with renal function was not attempted in the present study. *M. C. Berenbaum*

851. **Shwartzman Phenomenon in Fatal Infantile Diarrhoea due to *Escherichia coli* O–111, B4**
D. G. MCKAY and G. H. WAHLE. *Lancet* [*Lancet*] **2**, 1199–1200, Dec. 11, 1954. 2 figs., 15 refs.

Bacteriology

852. **Use of Color Change of Phenol Red as the Indicator in Titrating Poliomyelitis Virus or its Antibody in a Tissue-culture System**
J. E. SALK, J. S. YOUNGNER, and E. N. WARD. *American Journal of Hygiene* [*Amer. J. Hyg.*] **60**, 214–230, Sept., 1954. 3 figs., 7 refs.

In this paper from the University of Pittsburgh a method for titration of poliomyelitis virus and its antibody in human serum is described. This is as follows. A suspension of monkey kidney cells is made, by a method involving treatment with trypsin, and cultivated in glass tubes incubated at rest. The cells adhere to the glass surface. If growth occurs, the *p*H of the medium, which contains sodium bicarbonate and phenol red, falls from about 7·6 to about 6·6 in 6 to 8 days. The presence of active virus prevents growth and the consequent fall in *p*H. If virus dilutions or serum–virus mixtures are added before incubation, a change in colour of the phenol red during incubation indicates either the absence of active virus or its neutralization by antibody.

The titres of virus samples arrived at by this method agreed closely with those determined by their cytopathogenic effect on similar cultures. Antibody titres of human sera were about twice as high by the first as by the second method. Certain sera, when used in low dilutions, were found to have a toxic effect on the monkey cells, but this did not interfere with estimation of antibody titres higher than 1 in 16.

M. H. Salaman

BACTERIA

853. **The Isolation of Tubercle Bacilli from Sputum by Means of Detergents.** (L'isolement du bacille de Koch dans les crachats par les détergents)
F. TISON and A. LOZE. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **87**, 445–449, Oct., 1954. 8 refs.

The authors report that the treatment of tuberculous sputum with certain detergents has been successful in removing contaminating organisms rapidly without affecting the viability of the tubercle bacilli. Of 7 detergents investigated, " teepol ", 10% " bradosol ", and 15% laurylsulphate were the most effective, but the last-named had the serious disadvantage that it spoiled the culture medium. They describe their technique as follows: 1 ml. of sputum and 2 ml. of detergent are shaken mechanically for half an hour (1 hour for teepol) in a 50-ml., conical, stoppered, sterile tube, which is then filled with distilled water and shaken for a further half hour. After centrifuging, the water is removed, the deposit washed in more water, and finally inoculated on to 6 tubes of Jensen medium. The deposit obtained with teepol is oily, but can be transferred with a Pasteur pipette and spreads well; that produced by bradosol is compact and difficult to transfer. Preliminary treatment of the sputum with pepsin or papain was not found to produce liquefaction. In positive cases, colonies of tubercle bacilli appeared after about 12 days. The authors consider that this method is slightly less satisfactory than that using sodium carbonate, but note that after treatment of the sputum with teepol the colonies appeared somewhat sooner.

M. Lubran

854. **The Resistance of Tubercle Bacilli to Bactericidal Action of Benzalkonium Chloride (" Zephiran ")**
J. G. HIRSCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 312–319, Aug., 1954. 18 refs.

The bactericidal effect of several disinfectants on tubercle bacilli and on a group of non-acid-fast bacteria was investigated at the Rockefeller Institute for Medical Research, New York. It was found that several strains of tubercle bacilli—human, bovine, and avian, including virulent, avirulent, and attenuated strains—were resistant to benzalkonium chloride (" zephiran ") in a concentration of 0·1%, whereas this cationic detergent in a concentration of 0·005% was bactericidal for all saprophytic acid-fast and non-acid-fast bacteria tested. Its bacteriostatic effect was the same for the tubercle bacilli as for the other bacteria. Tubercle bacilli were isolated in pure culture from mixed bacterial suspensions after the mixtures had been treated with benzalkonium chloride. It is suggested that this detergent could be used in the culture of tubercle bacilli from materials, such as sputum, which are contaminated with other bacteria.

D. G. ff. Edward

855. **The Tubercle Bacillus in Tuberculous Lesions Treated by Resection after Chemotherapy. A Study of 97 Cases.** (Le bacille de Koch dans les lésions tuberculeuses traitées par exérèse après chimiothérapie. Une étude de 97 cas)
G. CANETTI, R. ISRAEL, P. HERTZOG, P. DAUMET, and L. TOTY. *Poumon* [*Poumon*] **10**, 465–485, June–July, 1954. 1 fig., 7 refs.

In an investigation carried out at the Pasteur Institute, Paris, fragments about 0·1 to 0·15 g. in weight from 381 lesions in 97 lungs or parts of lungs removed because of tuberculous infection were each treated, after grinding in a mortar, with 1·5 ml. of 4% sulphuric acid for 10 minutes; the acid was then neutralized with caustic soda, the suspension plated out on Löwenstein–Jensen medium, and the cultures examined repeatedly for *Mycobacterium tuberculosis* for 3 months.

Of the 381 cultures so examined, 185 (48·6%) were positive for tubercle bacilli and 164 (43%) were negative; the rest were invalidated by secondary infection. In 26 of the 97 cases none of the fragments tested yielded tubercle bacilli. Cultures from all cases of tuberculous pneumonia were positive and those from sclerotic lesions

commonly so, while those from draining lymph nodes were often positive even when the nodes were not caseous. Cultures from suspect patches in the lung parenchyma were often positive. In cultures made from tuberculous nodules the frequency of positive findings diminished as the lesions progressed towards healing, whereas it appeared to be unrelated directly to the duration of chemotherapy. The distribution of tubercle bacilli in tuberculomata was often not uniform through the different parts tested, and the organisms were most readily cultivated from liquefying tuberculomata and less often from softening or solid ones: again the duration of chemotherapy did not affect the result.

The successful cultivation of tubercle bacilli from cavities became less common as the cavity evolved; thus 91% of open evolving cavities gave positive results as against 63% of filled-up cavities, 47% of sclerocystic cavities, and 13% of full cavities. The concentration of bacilli in the cavities varied in much the same way. The duration of chemotherapy seemed to have a marked effect on the evolution of cavities.

The authors suggest that the tubercle bacilli present in nodules and tuberculomata divide infrequently and their metabolic activity is slight, so that chemotherapy has little effect, especially as these lesions are avascular. In cavities, on the other hand, the bacilli grow vigorously and chemotherapeutic agents are effective, so that the advanced, full cavity closely resembles a solid caseous lesion in its low content of bacilli.

(The eight remaining papers in this issue of *Poumon* all describe similar investigations carried out at other centres throughout France, their authors coming to much the same conclusions, while the findings are summed up in a concluding paper by Canetti. All the papers emphasize the frequency of lesions containing stainable but non-viable bacilli and the relatively large number in which no bacilli were detectable by any means. It is agreed on the whole that the degree to which bacilli can be cultivated from a lesion seems to depend on its development—the nearer the lesion is to scarring, the fewer viable organisms does it contain—and that the use of antibiotics seems to make little difference *per se* to the viability of the bacilli. In areas such as cavities where anatomical factors impede healing, viable bacilli tend to persist, their survival not being due to resistance to the antibiotics used in treatment. On the other hand the authors of one of the papers seem to be of the opinion that treatment with streptomycin and PAS, with or without isoniazid, favours sterilization of the lesions.

In his concluding remarks Canetti points out that the findings reported must be viewed in proper perspective, since most cases of pulmonary tuberculosis are treated by methods other than surgical excision—by rest and by collapse therapy of various kinds—and resort to surgical procedures is in most cases an admission of the failure of less drastic procedures. Moreover, although it may be true that the distribution of viable organisms in lesions of a particular kind is unaffected by treatment with antibiotics, this view neglects the possibility that the evolution of the lesions themselves may be determined by antibiotic therapy, and that this consequently determines the concentration of viable bacilli in the lung as a whole. In regard to cavities, indeed, the beneficial effect of antibiotics is generally conceded, and can be demonstrated by *x*-ray examination in many cases; the filling up of the mature cavity, which is encouraged by chemotherapy, in itself leads to sterilization of the tubercle bacilli in its contents.) *C. L. Oakley*

856. **Pathogenic Bacteria in Chronic Bronchitis**
J. R. MAY. *Lancet* [*Lancet*] **2**, 839–842, Oct. 23, 1954. 7 refs.

Sputum from patients with chronic bronchitis and from "infected asthmatics" was examined at the Institute of Diseases of the Chest, London, the main object being to determine the organisms responsible for the infection and hence the form of treatment likely to be of value. The majority of the granulocytes present in the sputum from asthmatics were eosinophils, and the response to treatment was directly related to the properties of neutrophil granulocytes also present. The author found that over the course of the last 2 years the incidence in truly purulent sputum of *Haemophilus influenzae* had increased from 24 to 90% and that of pneumococci had decreased from 71 to 20%; the interpretation of this finding is discussed. He confirmed his earlier observation that one or more potentially pathogenic bacteria can always be isolated from purulent or mucopurulent sputum. The fact that in certain cases sputum containing eosinophil "pus" is unaffected by antibacterial therapy has led to the routine cytological examination of sputum at the Institute.

The evidence presented suggests that *H. influenzae* is present in the sputum of 80 to 90% of patients with chronic bronchitis and that this should be the chief factor in determining the choice and dosage of the antibiotic used. *E. G. Rees*

857. **A Study of the Resistance of *Salmonella* to Chloramphenicol.** (Étude de la résistance des *Salmonellae* à la chloromycétine)
P. DU PASQUIER. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **87**, 418–426, Oct., 1954. 3 figs., 24 refs.

The author describes a method by which strains of enteric bacteria which are resistant to chloramphenicol have been readily produced by growing the freshly isolated organisms in the presence of varying amounts of the antibiotic and repeating the process, but selecting each time the organisms that have grown in the highest possible concentration of chloramphenicol. After 10 to 12 passages a strain of *Bacterium coli* initially resistant to a concentration of 9·4 μg. of chloramphenicol per ml. became resistant to one of 375 μg. per ml., and various strains of *Salmonella* to concentrations of 75 μg. to 2,000 μg. per ml. from an initial level of only 1·2 μg. to 4·7 μg. per ml.

The resistant strains were indistinguishable from non-resistant strains in respect of cultural appearance and biochemical reactions; most, however, were non-motile, and examination by phase-contrast microscopy showed marked pleomorphism, elongated forms being a marked feature. Flagellar staining showed that 25% of the organisms in the resistant strains were ciliated, compared

with 78% of the sensitive strains. The production of resistance was also accompanied by a change in the antigenic structure of the organism. In general, H antigen tended to disappear and Vi to become augmented. Resistance to the antibiotic began to disappear on repeated subculture in broth, on prolonged refrigeration, or on prolonged incubation, the organisms returning approximately to their initial level of sensitivity. During this process H antigen reappeared first, and then motility; the ciliated and elongated forms became less numerous and finally disappeared. *M. Lubran*

SEROLOGY AND IMMUNOLOGY

858. **The Metabolism of Antigen and Antibody**
F. J. Dixon. *Journal of Allergy* [*J. Allergy*] **25**, 487–503, Nov., 1954. 10 figs., 28 refs.

Recent experimental work carried out by the author and his colleagues at the University of Pittsburgh, in which the metabolism of antigen and antibody was studied by labelling certain protein fractions with radioactive iodine (^{131}I), is reviewed. Before antibody appears antigen is catabolized in the same way as the serum proteins of the host; with the appearance of antibody this catabolism becomes rapid. Antibody synthesis is rapid only in the presence of demonstrable amounts of antigen. Prolonged low-level antibody production probably depends more upon repeated exposure of the host to the antigen than upon retention of traces of antigen in the body. Antibody production can possibly be separated into two phases: one of short duration, lasting perhaps only a few hours, which can be influenced by *x*-irradiation or by administration of cortisone, and a second, longer one which is insensitive to both these factors.
H. Herxheimer

859. **Rickettsial-interference Phenomenon: a New Protective Mechanism**
W. H. Price, J. W. Johnson, H. Emerson, and C. E. Preston. *Science* [*Science*] **120**, 457–459, Sept. 17, 1954. 3 refs.

[This is a short technical and rather speculative account of interference protection in rickettsial infections which must be read in the original by those interested.]
G. Payling Wright

860. **Specific Prophylaxis of Mumps (Preliminary Communication).** (Специфическая профилактика свинки)
A. A. Smorodintsev and N. S. Klyachko. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 6–11, No. 11, Nov., 1954. 3 figs.

At the Pasteur Institute, Moscow, 4 strains of mumps virus isolated during 1950 from the pooled saliva of 10 patients and one strain isolated from the cerebrospinal fluid of another patient were attenuated by 17 to 40 passages through chick embryos to the extent that they had lost all infectivity for human subjects. The intracutaneous injection of a monovalent vaccine prepared in this way into a subject who had not previously had mumps resulted in a 16-fold increase in the serum titre of neutralizing antibodies and an 8-fold increase in that of complement-fixing antibodies, whereas another subject, who had a previous history of mumps, showed only a 4-fold increase in titre of the complement-fixing antibodies.

A polyvalent vaccine prepared from all 5 strains was then given intradermally to 39 adults, all of whom showed a small local reaction, but no other symptoms. The serum titre of neutralizing antibodies increased to 2 to 8 times its previous value in 30 (76·9%) and that of complement-fixing antibodies to a similar degree in 34 (87·5%) of those inoculated. Those subjects with a low initial titre showed, on the average, the greatest increase and vice versa.

The authors propose to test this method of vaccination in older children before applying it on a large scale in nurseries threatened by an outbreak of mumps.

[Unfortunately, no credit is given to the pioneer work in this field of Enders and his colleagues during the years 1942–6.] *K. S. Zinnemann*

861. **An Experimental Investigation into the Prophylactic Value of Influenza Vaccine, as Used during the Winter of 1952–1953.** (Een experimenteel onderzoek naar de waarde van de vaccinatie tegen influenza in de winter 1952/1953)
J. D. Verlinde and O. Makstenieks. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 2589–2591, Sept. 11, 1954. 4 refs.

In view of the poor results obtained in a large-scale test of vaccination against influenza in 1953 (*Ned. T. Geneesk.*, 1954, **98**, 559; *Abstracts of World Medicine*, 1954, **16**, 77) experiments were undertaken at the Netherlands Institute of Preventive Medicine, Leiden, on mice to determine how far this was attributable to the fact that the strain of influenza virus responsible for the epidemic in the winter of 1952–3, although of Type A_1, was not identical with either of the Type-A_1 strains (FM_1, Liverpool) from which the vaccines used in the trials were prepared. It was found that the susceptibility of animals similarly vaccinated was slightly diminished to the FM_1 strain, but was unchanged in relation to the new (Vr) strain, and that no heterologous antibodies to the Vr strain appeared. Such protection as was afforded against the FM_1 strain was only of a few weeks' duration. *R. Crawford*

862. **Apparent Failure of Chick-embryo-adapted Hepatitis Virus to Immunize against Natural Virus**
C. I. Leftwich, G. S. Mirick, and G. Henle. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 559–570, Oct., 1954. 6 figs., 31 refs.

Oral administration of chick embryo material presumably containing infectious hepatitis virus produced in volunteers a disease compatible with a very mild hepatitis. No evidence was obtained of the development in the volunteers of immunity to unadapted virus under the conditions of the experiment. Various possible explanations for these results are discussed.—[Authors' summary.]

Pharmacology

863. **Anthelminthic Properties of Water-melon Seeds.** (О противоглистных свойствах семян арбуза)
I. M. Fefer, M. Z. Mindlin, and N. N. Prokopovich. *Фармакология и Токсикология* [*Farmakol. i Toksikol.*] 17, 50–51, Sept.–Oct., 1954.

Whereas the anthelminthic properties of the seeds of the pumpkin (*Cucurbita maxima*) have been known since antiquity, those of the water melon (*Citrullus vulgaris*) have not apparently been used for this purpose. Investigations at the Kiev Institute of Pharmacology demonstrated that watery extracts of water-melon seeds paralysed the cat tapeworm in 20 minutes (in 1 : 10 concentration), while alcoholic extracts of the seed shells had a similar effect on cat tapeworms and roundworms within 30 minutes. Water-melon-seed oil paralysed both these types of worm in 10 minutes, but ether extracts had no anthelminthic properties. *A. Swan*

864. **Antagonistic Effect of A.C.T.H. and Cortisone on the Anticoagulant Activity of Ethyl Biscoumacetate**
J. B. Chatterjea and L. Salomon. *British Medical Journal* [*Brit. med. J.*] 2, 790–792, Oct. 2, 1954. 2 figs., 11 refs.

In an investigation of the causes of a high incidence of thrombo-embolic complications during administration of ACTH (corticotrophin) or cortisone, 2 female patients, one suffering from acquired haemolytic anaemia and the other from acute thrombophlebitis, were studied at Tufts College Medical School, Boston. ACTH was given in a dose of 80 to 100 mg. subcutaneously every 6 hours until the full therapeutic effect had been obtained, 20 to 25 mg. being given daily thereafter as a maintenance dose. Cortisone, in a dose of 150 to 200 mg., was administered orally or intramuscularly, the maintenance dose usually being one-quarter of this amount. Ethyl biscoumacetate (" tromexan ") was given daily in amounts varying from 300 to 1,200 mg., the exact requirement being judged from the plasma prothrombin activity, which was determined by a slight modification of the method of Quick; the plasma prothrombin conversion factor (P.P.C.F., labile factor) and the plasma fibrinogen levels were also determined.

The patient with haemolytic anaemia had developed thrombophlebitis during the administration of 100 mg. of cortisone daily. The serum contained auto- and iso-erythrocyte antibodies and the Coombs test was positive. On the institution of anticoagulant therapy wide fluctuations of prothrombin activity were noted. When the cortisone was discontinued a satisfactory therapeutic level of plasma prothrombin activity was easily obtained. Resumption of cortisone therapy was followed by a rise in plasma prothrombin activity, and the dose of ethyl biscoumacetate had to be increased to maintain a therapeutic level. Whereas the P.P.C.F. level showed no significant change, the plasma fibrinogen level, which had been high before the start of cortisone therapy, fell to normal levels on clinical and haematological improvement. In the second patient, who had acute thrombophlebitis, ACTH was found to increase the amount of ethyl biscoumacetate required to obtain an effective plasma prothrombin level, the requirement of anticoagulant falling again on decreasing the dose of ACTH.

The mechanism of this phenomenon is not clear, but some possibilities are discussed. Meanwhile the authors recommend that, unless absolutely indicated for their known specific effects, ACTH and cortisone should be withheld in the presence of thrombo-embolic complications. *Norval Taylor*

865. **A New Carbohydrate-iron Haematinic for Intramuscular Use**
D. F. Cappell, H. E. Hutchison, E. B. Hendry, and H. Conway. *British Medical Journal* [*Brit. med. J.*] 2, 1255–1257, Nov. 27, 1954. 2 figs., 10 refs.

The authors report, from the Western Infirmary, Glasgow, the successful results of the clinical trial of a new dextran–iron complex (" imferon "), which was administered to 15 patients suffering from iron-deficiency anaemia. The haemoglobin values ranged from 29 to 66% (14·8 g. Hb per 100 ml. being taken as 100%), and the diagnosis of iron-deficiency anaemia was based on three criteria: a low mean corpuscular haemoglobin concentration, a low serum iron level, and an absence of stainable iron in the sternal marrow. As one patient died from cerebral embolism shortly after treatment began, only 14 patients were followed for a period sufficient for assessment of the haematinic effectiveness of the preparation; of these, 6 were known to be refractory to ferrous sulphate by mouth and 2 had shown marked intolerance of it. During a control period, varying from 7 to 16 days, 2 to 5 specimens of blood from each case were examined to ensure that no significant fluctuations in haemoglobin value occurred. The dosage of imferon was 4 ml. (200 mg. of elemental iron) given intramuscularly every other day into alternate buttocks.

In all cases a satisfactory rise in the haemoglobin level took place, although the rate with which this occurred varied; the factors causing the variation have not yet been determined. Over the whole series the average increase in haemoglobin value during the first month of treatment varied from 0·51 to 1·67 g. per 100 ml. (3·5 to 11·3%) per week. A significant rise in the serum iron content was demonstrable less than 18 hours after the first injection, and the reticulocyte count had increased by 12% by the sixth day. No attempt was made to assess accurately the degree of utilization of the iron injected, but from the figures available this seemed to be over 80% in some cases. In no instance was the injection followed by any general reaction, and no more than slight local tenderness was experienced. In 2

patients who showed staining of the skin in the areas of injection the pigmentation appeared within 24 hours of the injection and was first thought to be a bruise; its true nature, however, became apparent later when the colour changed to a slate-grey, resembling the skin pigmentation of idiopathic haemochromatosis. Pigmentation was still obvious, although less intense, 4 months after completing treatment. In one case a small piece of the skin was removed for histological examination at 3 months; this showed iron pigment to be abundant in the phagocytes in the corium and the melanin in the overlying epithelium to be increased. Although no case of sensitization occurred during this trial the authors have been informed of a case in which urticaria developed immediately after the injection. The death of one patient provided the opportunity of studying the route of absorption, which was shown to be by the lymphatics.

The indications for treatment with intramuscular iron are considered to be the same as those for intravenous iron, that is, intolerance or refractoriness to iron by mouth, or the necessity for a rapid response, either in pregnancy or in preparation for operation. The authors point out that the long-term effects of parenteral iron overdosage in human subjects are not yet fully understood, and although the deposit of moderate amounts of surplus iron in the tissues does not in itself seem to be notably harmful, they stress that it is undesirable to administer this or any other parenteral remedy when it is not required. *Robert Hodgkinson*

866. **Action of Promethazine on Systemic Blood Pressure, Pulmonary Artery Pressure, and Pulmonary Blood Flow**

S. HOWARTH and S. G. OWEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1266–1267, Nov. 27, 1954. 4 refs.

Promethazine hydrochloride (" phenergan ") has been recommended for use in association with a barbiturate or pethidine as a sedative before the performance of cardiac catheterization. The authors have therefore investigated the effect of this drug on the circulation in 3 cases of mitral stenosis, 2 of atrial septal defect, and one of dilated aorta undergoing diagnostic cardiac catheterization at the National Heart Hospital, London. All except one of the patients were given 3 grains (0·2 g.) of sodium amylobarbitone by mouth. The pulmonary and brachial arterial pressures were measured continuously by means of capacitance manometers, blood samples for gas analysis were taken simultaneously from the pulmonary and brachial arteries, and oxygen consumption was measured both during the control period before the intravenous injection of 50 or 25 mg. of promethazine and after the last blood sample was taken, the second estimation being used to calculate the pulmonary blood flow after administration of the drug. The heart rate was determined from electrocardiographic records taken throughout the period of observation. The control period lasted approximately 20 minutes, and the experimental period 17 to 22 minutes after the injection of promethazine.

The authors conclude that the drug has little effect on the circulation in the doses used, the only consistent feature observed being a mild tachycardia. It did increase sedation, but this was accompanied in 2 cases by disorientation and inability of the patients to cooperate. *P. A. Nasmyth*

867. **Studies with Dilatol, a Vasodilator Substance**

A. G. RIDDELL, M. STEEL, and J. M. MCCOY. *Angiology* [*Angiology*] **5**, 314–317, Aug., 1954. 2 figs., 6 refs.

The effect of " dilatol " (1-(*p*-hydroxyphenyl)-2-1-methyl-3′-phenyl propylamino)-propanol hydrochloride), a vasodilator substance, on healthy adults was studied at University College Hospital, London. The drug was given, either by intramuscular injection in a dose of 5 mg. or by mouth in a dose of 10 mg., on 29 occasions to 20 healthy men aged 20 to 25 years. Eight minutes after the oral dose the diastolic pressure began to fall, reaching a minimum of 35 mm. Hg in about 23 minutes; it then rose gradually, becoming normal about an hour after administration of the drug. The systolic pressure remained constant. There was a rise in the pulse pressure from a resting value of 50 mm. Hg to a maximum of 85 mm. Hg; but there was only a slight concomitant increase in the pulse rate. With intramuscular injection a fall in diastolic pressure was observed after much the same interval as when the drug was given by mouth, indicating that by the latter route the drug was very rapidly absorbed. There was little difference between the two routes of administration in the degree of change induced, except that the maximum effect on pulse pressure was slightly greater after intramuscular injection than after oral administration. Investigation of skin temperature and of tissue blood flow indicated that in man the main effect of dilatol is on the skin vessels rather than on the muscle vessels. No severe side-effects were observed, but mild palpitation was common, and at the end of the investigation a few subjects had symptoms of mild postural hypotension.

It is concluded that dilatol is a safe vasodilator with a rapid and regular action even when given by mouth. *Adrian V. Adams*

868. **Elimination of Periplocymarin.** (Элиминация периплоцимарина)

P. I. ONITSEV. *Фармакология и Токсикология* [*Farmakol. i Toksikol.*] **17**, 45–48, Sept.–Oct., 1954. 3 refs.

Periplocymarin is a new cardiac glucoside obtained from *Periploca graeca* L., a plant common in the Caucasus. It can be crystallized in the form of glistening needles which are readily soluble in alcohol, but not in water. Its melting point is 148° C., and its formula is $C_{30}H_{46}O_8$. Periplocymarin resembles cymarin, a component of strophanthin, and also gives a positive Keller–Kiliani reaction. It is highly active, containing 2·703 cat units per gramme, its absorption and excretion are rapid, and its cumulative effects consequently negligible.

In the work here reported from the Kharkov Chemico-pharmaceutical Research Institute the elimination of periplocymarin was investigated in 41 cats by studying the effect on the lethal dose of changes in the rate of administration. The critical rate of infusion was found to be 0·036 mg. per kg. body weight per hour, and the rate of its elimination 0·014 to 0·016 mg. per kg. per hour.

It was confirmed that the cumulative effects of periplocymarin were less marked than those of other cardiac glucosides. *A. Swan*

869. **The Influence of Antipyretics on Intestinal Secretion in Health and during Experimentally Induced Fever.** (Влияние антипиретиков на кишечную секрецию в норме и при экспериментальной лихорадке)

V. B. Isachenko. *Бюллетень Экспериментальной Биологии и Медицины* [*Byull. eksper. Biol. Med.*] **38**, 25–29, Oct., 1954. 2 figs., 6 refs.

At the Institute of Experimental Medicine, Leningrad, quantitative estimations were made in 4 dogs with isolated intestinal loops of the effect on intestinal secretion of mechanical stimulation (insertion of a drainage tube into the fistula), the administration of calomel (0·3 g. in 5 ml. of saline for 5 minutes in the isolated loop), and of the antipyretics phenacetin and amidopyrine. A total of 173 experiments were carried out.

These showed that phenacetin and amidopyrine given to healthy dogs, apart from lowering the temperature by 0·5 to 1·3° C., exerted a depressing effect on the reflex secretion of the intestinal glands which lasted at least 4½ hours; hypersecretion of the isolated intestinal loop induced by calomel was similarly depressed. The action of phenacetin was more pronounced than that of amidopyrine. Leptazol was found to have no antagonistic action to the depressive effect of phenacetin on calomel-induced intestinal hypersecretion. When pyrexia was induced by injection of an autoclaved culture of *Bacillus subtilis* it produced a considerable depression of intestinal secretory activity, this depression being demonstrated to occur even before the rise of temperature. Phenacetin and amidopyrine restored to normal the secretory activity, as well as the calomel-induced hypersecretion, their action on the bowel being more rapid than that on the temperature-regulating centre. *A. Swan*

870. **Effect of Antitussive Agents on Experimental and Pathological Cough in Man**

J. S. Gravenstein, R. A. Devloo, and H. K. Beecher. *Journal of Applied Physiology* [*J. appl. Physiol.*] **7**, 119–139, Sept., 1954. 7 figs., 13 refs.

The comparative value of heroin (diamorphine hydrochloride), dextromethorphan, morphine, and codeine in the suppression of experimental and pathological cough in man was studied at the Massachusetts General Hospital (Harvard Medical School), Boston. Three methods were used to produce experimental cough: (1) inhalation of 2% ammonia gas, (2) inhalation of 5% or 10% citric acid mist, and (3) intravenous injection of 0·25 to 0·5 ml. of paraldehyde. In none of these experiments were the customary (or even unusually large) doses of the agents tested (with the exception of heroin) consistently effective in significantly diminishing the frequency of coughing.

Pathological cough was then observed in two groups of male and female patients, most of whom were suffering from pulmonary tuberculosis and had a productive cough of at least 2 months' duration. Group A were given 3-day oral courses of codeine (10 mg.), dextromethorphan (10 mg.), heroin (5 mg.), and a placebo of lactose (50 mg.) in random order with intervals of one day between courses. Group B were given similar courses of codeine (15 mg.), N-allylnormorphine (20 mg.), narcotine (5 mg.), and the lactose placebo. In these studies the reduction in cough was so slight as not to be statistically significant. Patients in Group A could distinguish between the effects of codeine and heroin and those of dextromethorphan or lactose, and had the impression that the first two agents reduced cough frequency when in fact they did not significantly reduce it, the drugs having so altered the patients' subjective appreciation as to lead them to believe that objective improvement had occurred. Patients in Group B failed to distinguish antitussive agents correctly, suggesting that the effect of these drugs was very small.

The fact that patients request antitussive agents therefore depends on qualities other than their effectiveness in reducing cough frequency. In a lengthy discussion the authors suggest that euphorigenic or hypnotic effects may play an important part in producing relief by facilitating adaptation to irritation, particularly in those used to these agents. They believe that this aspect requires further study, which should include non-narcotic classes of drugs. In view of the importance of subjective factors in the evaluation of antitussive remedies, the authors do not feel that the study of cough produced experimentally in normal subjects will be helpful except in the assessment of the hypnotic power, euphorigenic qualities, and toxic effects of the agents investigated, and conclude that in the study of applied pharmacology the sick man is the only satisfactory experimental subject. *I. Ansell*

871. **The Effect of Painful Impulses on the Sensitivity of White Mice to Certain Therapeutic Substances.** (О влиянии болевых раздражений на чувствительность белых мышей к некоторым лекарственным веществам)

S. G. Kuznetsova. *Фармакология и Токсикология* [*Farmakol. i Toksikol.*] **17**, 48–50, Sept.–Oct., 1954. 2 figs., 4 refs.

The action of certain analeptics (ephedrine, cocaine, strychnine, and "phenamin") on white mice was studied at the Saratov Medical Institute: (1) in intact animals; (2) in animals subjected 10 to 15 minutes after the subcutaneous injection of the analeptic to a painful stimulus such as a subcutaneous injection of ether, scalding of the tail, or the application to the tail of three ligatures; and (3) in animals under "barbamil" sedation.

It was established that painful stimuli, irrespective of their nature, increased the lethal effect of these analeptics. Thus injections of one-half of the maximum tolerated dose for control animals caused a mortality of 20 to 30% in mice subjected to trauma, while with doses which killed 40 to 50% of the control animals the mortality rose to 80 to 90% after trauma. Light sleep induced with barbamil reduced the above mortality of 80 to 90% to 10 to 20%, but deep sleep was found to be far less effective in this respect. *A. Swan*

Chemotherapy

872. **Intramuscular Oxytetracycline**
C. P. SCHLICKE and W. E. ANDERSON. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 939–943, Sept., 1954. 7 refs.

A total of 110 patients, mainly in hospital for surgical treatment, received 100 mg. of oxytetracycline intramuscularly every 12 hours with good effect on a variety of infections. No untoward systemic effects were noted, and pain after injection was complained of by only 21 patients. Local reactions were not severe, and no suppuration occurred. *T. Anderson*

873. **Clinical and Pharmacologic Studies of Intramuscular Oxytetracycline**
W. S. WADDINGTON, T. B. SMART, and W. M. M. KIRBY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 1037–1044, Oct., 1954. 7 refs.

One hundred patients were treated with a new preparation of oxytetracycline designed for intramuscular injection. Patients receiving 100 to 200 mg. every 8 hours had serum concentrations of the antibiotic comparable to those obtained by giving 0·25 to 0·5 g. orally every 6 hours. The injections were well tolerated by the majority of patients receiving 100 mg. every 8 hours. Increasing the dose to 200 mg. every 8 hours resulted in a substantially higher incidence of pain at the injection site and did not yield significantly higher serum concentrations. Induration of the tissues occurred in only one patient in whom the injections were given too superficially. Gastrointestinal side reactions were rare, occurring in only one patient.

Clinical results in patients with bacterial pneumonia, peritonitis, and other infections as well as in patients receiving the antibiotic as prophylaxis following surgical operations were entirely comparable to those obtained with oxytetracycline administered by mouth or by intravenous injection.

The chief advantage of the intramuscular preparation is that it can be used in patients in whom oral or intravenous therapy is inconvenient or impossible. It is indicated mainly in patients who are combative or vomiting, in infants, and in the postoperative management of surgical patients.—[From the authors' summary.]

874. **Routine Testing of the Bactericidal Action of Antibiotics for Clinical Purposes.**
G. R. F. HILSON and S. D. ELEK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 589–594, Oct., 1954. 1 fig., 13 refs.

The authors describe a method developed at St. George's Hospital Medical School, London, for the assessment of the bactericidal action of drugs *in vitro*. "Primary" plates are inoculated by flooding with broth cultures of the organism to be tested. Blotting-paper disks are then placed on the surface of the plates, which are incubated for 18 to 24 hours, zones of inhibition developing in the usual way. A disk of sterile velvet (mounted on a wooden backing) is now pressed, first on the surface of the "primary" plate and then on the surface of a sterile nutrient-agar plate, which is incubated overnight. In this way a mass subculture is made from the "primary" plate containing antibiotics on to a "replica" plate free of drugs, on which any viable bacteria can multiply.

The results of tests made in this way of the bactericidal action of 7 antibiotics on 65 bacterial strains were broadly in agreement with those obtained by other techniques, and it is suggested that this method may be of value in routine laboratory work.

A. W. H. Foxell

875. **Clinical Trials of *o*-Diazoacetyl-L-serine ("Azaserine") in Neoplastic Disease**
R. R. ELLISON, D. A. KARNOFSKY, S. S. STERNBERG, M. L. MURPHY, and J. H. BURCHENAL. *Cancer* [*Cancer (N.Y.)*] **7**, 801–814, July, 1954. 1 fig., 15 refs.

It has been shown that the serine analogue, *o*-diazoacetyl-L-serine ("azaserine"), an antibiotic isolated from a broth culture of a *Streptomycete*, inhibits the growth of transplantable neoplasms in mice. In this paper from the Memorial Center for Cancer and Allied Diseases and the Sloan-Kettering Institute, New York, clinical trials of azaserine against human neoplasms are described, a crude preparation from the streptomycete culture being used at first, and then the natural crystalline and finally synthetic azaserine as these became available. Altogether 93 separate trials were carried out on 41 adults and 15 children with various forms of neoplastic disease, the drug being administered until definite signs of toxicity appeared.

Toxic effects, which appeared after 5 to 20 days (total dose between 50 and 200 mg.), principally involved the digestive tract, with redness of the tongue and buccal mucosa, which sometimes became ulcerated, and nausea and vomiting. These symptoms improved rapidly when administration of the drug ceased. The most serious toxic effects were systemic intoxication, with anorexia, weakness, apathy, and serum electrolyte disturbances, and jaundice, which occurred in 9 adults. These complications were noted only in patients in poor condition; they could not, therefore, be attributed with certainty to the effects of the drug; they were not observed in children.

The therapeutic results of administration of azaserine were limited to a decrease in fever during the period of treatment in 7 out of 19 patients with Hodgkin's disease and brief periods of objective improvement in 5 others with this disease; a decrease in the leucocyte count in 2 cases of lymphatic leukaemia; and brief partial haematological remissions in 3 out of 14 children with acute leukaemia. *L. A. Elson*

Infectious Diseases

876. **Tasks in the Fight against Influenza in the Light of the Latest Findings.** (Задачи борьбы с гриппом в свете новейших данных)
A. A. Smorodintsev. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 22–33, No. 9, Sept., 1954.

[This paper, which forms the main contribution to a special symposium on influenza consisting, in all, of 10 papers (some of which are abstracted below), provides a survey of the present position of the influenza problem and of developments to be expected in the immediate future in the U.S.S.R. by one of the leading Soviet authorities on the influenza virus. Among a number of facts that are equally well known and established in Western countries, some indications can be discerned of developments differing from the pattern with which we are familiar. Unfortunately no references are given to any of the many publications quoted.]

Epidemiological surveys carried out since 1936 in the main population centres of the Soviet Union have shown that major outbreaks of influenza were due to virus of Types A and B in earlier years and of Types A′ and B′ since 1949. However, Types A and B have also been isolated during outbreaks due principally to Types A′ and B′ and vice versa, while serological investigations have usually shown a rise in titre of antibodies to all types of the virus, though more markedly to the type prevalent at a given moment. The conclusion drawn from these findings is that for mass immunization only polyvalent vaccines are likely to be of value. Before the effect of any such vaccine can be assessed on a large scale, however, it is necessary to improve and simplify diagnostic procedures so as to enable epidemiologists to distinguish between true virus influenza and acute catarrh of the respiratory tract. For this purpose, in addition to the haemagglutination-inhibition and complement-fixation reactions, the technique of rhinocytoscopy developed by Kolyeditskaya is of value [see Ostapkovich, *Vestn. Oto-rino-laring.*, No. 2, 1953, 19; *Abstracts of World Medicine*, 1953, **14**, 356]. In this procedure specially ground glass slides are used to take impression preparations from the nasal mucosa which are stained and examined. Whereas preparations from healthy subjects consist mainly of leucocytes and single epithelial cells, in virus influenza conglomerations of cylindrical ciliated epithelial cells are found, the cytoplasm of which frequently contains azurophilic and oxyphilic inclusion bodies presumably representing colonies of the virus. These inclusion bodies have been demonstrated regularly in large numbers of preparations made during epidemics in the years 1949–52, and the method has been found to give a higher rate of positive results than the serological methods. Conglomerations of ciliated epithelial cells may also be found in certain cases of simple chronic infection of the nasal mucosa, but in these cases the inclusion bodies are absent.

Active immunization by mass vaccination was tested during the period 1937–52 in 9 experiments involving altogether about 300,000 subjects. The polyvalent vaccines used contained living, modified virus of Types A and B, to which later Type A′ was added. The vaccines were prepared from chorio-allantoic cultures by drying *in vacuo*, and were administered intranasally, either in powder or fluid form, in 2 doses. The virus could be recovered from the nasopharynx for 3 to 4 or more days after the first dose, whereas after the second dose isolation of the virus was no longer possible. Serum antibody titres were increased to 5 to 8 times their former level after successful immunization. These mass immunization experiments are regarded as providing a severe test, since the immunized subjects lived in the midst of a completely unprotected population. But even under these conditions it was found that vaccination reduced the over-all incidence of virus influenza by half; in one well-controlled experiment involving 60,000 subjects the incidence of infection amongst the vaccinated was less than one-third of that amongst the unprotected population.

Equally good or even better results have been obtained [but apparently with only small numbers of subjects] with passive immunization, either with immune serum from horses or with serum from immunized human donors. The serum was introduced intranasally as a fine spray either in the fluid or dried state, spraying being carried out once during non-epidemic and twice, at weekly intervals, during epidemic periods. The incidence of virus influenza among subjects thus passively immunized was one-third to one-fourth of that in the non-immunized.

K. S. Zinnemann

877 (*a*). **The Significance of Type-A′ Virus in the Epidemic Process of Influenza.** (Значение вируса A′ в эпидемическом процессе при гриппе)
N. R. Gutman and L. Mentkevich. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 38–43, No. 9, Sept., 1954.

877 (*b*). **Changes in the Antigenic Structure of Influenza Virus A and A′ in the Course of Five Years.** (Изменение антигенной структуры вируса гриппа A и A′ на протяжении пяти лет)
V. V. Ritova and L. Y. Zakstel'skaya. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 43–49, No. 9, Sept., 1954. 2 figs.

In the first of these two papers the authors describe investigations carried out at the Tarasevich Institute, Moscow, on a number of virus strains isolated during November and December, 1953, when a widespread outbreak of influenza occurred, and which were considered to be related to the Type-A′ virus isolated during 1949–52. On the other hand cross-neutralization reactions between animal antisera produced with the old and new strains and between patients' sera showed there to be certain antigenic differences between the two.

The second paper, from the Institute of Virology of the Armenian S.S.R., also describes the serological comparison of strains isolated during 1953 with Type-A′ strains isolated in previous years. The authors come to the conclusion that three sub-types may be identified among the former: (1) strains similar to Type-A′ strains isolated in 1949 and 1952; (2) strains differing considerably from the 1949 and 1952 Type-A′ strains, as shown by differences in titre; and (3) Type-A′ strains giving no cross-reactions at all with Type-A strains. These findings are held to support the hypothesis that Type-A virus possess a certain plasticity, and that contact with Type-A antibodies and possibly other factors during its circulation among the immune population produces antigenic changes resulting in the appearance of intermediate types. Type-B virus is regarded as not being so plastic as Type A, although the authors note that one Type-B strain isolated in 1953 agglutinated only to one-eighth, and another isolated in 1950 only to one-quarter, of the titre obtained with a Type-B strain dating from 1940. *K. S. Zinnemann*

878 (*a*). **Efficacy of Mass Vaccination against Influenza.** (Об эффективности массовой вакцинации против гриппа)
S. A. Samvelova. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 9–13, No. 9, Sept., 1954. 1 fig.

878 (*b*). **Efficacy of Anti-influenzal Inoculation with Formol-killed Vaccine Containing a Stimulator (Orlova's Vaccine)** (Эффективность противогриппозных прививок убитой формол-вакциной со стимулятором)
S. L. Shapiro, V. D. Russina, I. I. Chekunova, V. G. Nedosekin, and K. L. Birnbaum. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 13–15, No. 9, Sept., 1954.

878 (*c*). **Immunization Results with Shdanov's Living Anti-influenzal Vaccine.** (Данные по иммунизации против гриппа живой вакциной Жданова)
S. I. Topolyanskaya, M. S. Lëv, E. I. Lurina, A. A. Berenshtein, and M. A. Gerasimov. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 16–20, No. 9, Sept., 1954.

878 (*d*). **The Problem of the Efficacy of Anti-influenzal Vaccination.** (К вопросу об эффективности противогриппозной вакцинации)
R. G. Balakireva and N. S. Kropotova. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 20–22, No. 9, Sept., 1954.

These four papers give an account of the results of active immunization against influenza with four different polyvalent vaccines in different districts of Moscow during 1953–4, the first paper providing a general survey by the City Public Health Department, while the others give the results for the three most thickly populated districts in detail. In all, 629,438 people were vaccinated intranasally: (A) 410,986 with a vaccine prepared by the Institute of Virology; (B) 81,094 with Orlova's formol-killed vaccine reinforced with a "stimulator" (bile); (C) 70,475 with a fluid vaccine prepared by the Metchnikov Institute; and (D) 66,883 with a vaccine in powder form prepared by the Institute of Experimental Medicine.

Inoculation with Vaccines A, C, and D reduced the incidence of influenza by 21 to 51% and with Vaccine B by 3 to 20%. The authors of the paper dealing with Vaccine B claim that the comparatively poor results obtained with this type of vaccine were attributable to an unusually high incidence of the disease in the area in which it was used. With Vaccine C on the other hand the efficacy of vaccination was doubled where the incidence of the disease was high. *K. S. Zinnemann*

879. **Aseptic Meningitis Caused by Coxsackie Virus with Isolation of Virus from Cerebrospinal Fluid**
K. Hummeler, D. Kirk, and M. Ostapiak. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 676–679, Oct. 16, 1954. 11 refs.

An outbreak of aseptic meningitis in which the causative organism was found to be a Coxsackie virus occurred in an institution for mental defectives at Elwyn, Pennsylvania, during July, 1953. In the 11 patients observed the onset was sudden, with muscular pains and clinical evidence of meningeal involvement. The cerebrospinal-fluid cell count ranged from 22 to 99 cells per c.mm., with a predominance of lymphocytes. Blood, cerebrospinal fluid, and material prepared from faeces and throat swabs were inoculated into suckling mice and into roller-tube tissue cultures of Strain HeLa cells.

Coxsackie virus Group B, Type 2 (Ohio) was isolated from specimens of faeces in 4 cases, from a throat swab in one case, and from spinal fluid in one case. Complement-fixation and neutralization tests with prototype and homologous viruses and patients' sera supported the conclusion that the epidemic was caused solely by this particular Coxsackie virus. No poliomyelitis virus or other Coxsackie virus was isolated. Two strains of Coxsackie B_2 virus caused cytopathogenic effects in roller-tube tissue cultures. *D. Geraint James*

880. **Jamshedpur Fever. A Preliminary Report**
N. Khan. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **8**, 597–609, Sept., 1954. 3 figs., 4 refs.

An epidemic of febrile encephalitis occurred in Jamshedpur during 1954, and in this paper the author reviews the clinical and preliminary laboratory findings. Severity of onset and the clinical course permitted arbitrary division into 4 types of case: fulminating, toxic, relapsing, and abortive. About one-half of the total of 400 patients, including the 14 who died, were under 15 years of age. Failure to demonstrate any aetiological agent and lack of response to broad-spectrum antibiotics suggested that the disease might be a virus encephalitis; this hypothesis is being investigated locally and at the Virus Research Centre, Poona, and the findings are to be the subject of a future communication. The cerebrospinal fluid (C.S.F.) showed no pleocytosis, but there was a polymorphonuclear leucocytosis in the peripheral blood. A significant feature in severe cases was a low blood sugar level with a correspondingly low sugar content of the C.S.F.; in all such cases glucose was given intravenously. *D. Geraint James*

Tuberculosis

881. **The Treatment of Tuberculous Meningitis without Intrathecal Therapy**

J. M. SMELLIE. *Lancet* [*Lancet*] **2**, 1091–1093, Nov. 27, 1954. 4 figs., 13 refs.

One of the serious disadvantages of streptomycin therapy in the treatment of patients suffering from tuberculous meningitis has been the need to give intrathecal injections for many weeks or months. Since the introduction of isoniazid, however, it is the general experience that by using this drug in combination with streptomycin the number of intrathecal injections of streptomycin required has been reduced. In this paper from the Birmingham Children's Hospital the results of treating 15 children suffering from tuberculous meningitis with streptomycin given intramuscularly and isoniazid given by mouth, but without intrathecal injections, are recorded.

The patients were given streptomycin intramuscularly in the generally accepted dosage (20 mg. per lb. (44 mg. per kg.) body weight daily) for periods of 3 to 5 months and isoniazid orally in a dosage of 4 mg. per lb. (8·8 mg. per kg.) daily for about 5 months. The patients were unselected, but most of them were in the early stage of the disease and bacteriological proof was not forthcoming, although the changes in the cerebrospinal fluid conformed to the accepted diagnostic criteria. The period of follow-up was short (5 months) in some cases and in others as long as 25 months. Few details are given, but 13 of the 15 patients showed " an eminently satisfactory result ", 1 child died, and 1 is mentally and physically retarded. The author refers, but not in detail, to the experience of other investigators which, he states, provides " further evidence in favour of the use of oral isoniazid in tuberculous meningitis " [but the implication that this evidence supports the contention that the treatment of tuberculous meningitis without intrathecal therapy gives as good results as with intrathecal therapy has since been challenged by Illingworth and Lorber (*Lancet*, 1954, **2**, 1229), who point out that " in 5 of the 7 quoted papers intrathecal treatment was in fact given to some or to all patients"].

[While this paper encourages the hope that in selected cases it may be possible and desirable to dispense with intrathecal streptomycin, it should be emphasized that in most cases, especially in young babies in an advanced stage of the disease, it is still necessary to give intrathecal therapy. There is a need for a controlled trial to assess more critically the value of intrathecal streptomycin in patients with tuberculous meningitis who are receiving intramuscular streptomycin and oral isoniazid therapy.]

R. M. Todd

882. **Treatment of Bone and Joint Tuberculosis with Streptomycin and P.A.S. (A Follow-up Study.)** [In English]

J. HALD. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **30**, 82–104, 1954. 37 figs.

883. **Primary Tuberculosis of the Lung. Analysis of 298 Cases of Primary Complex Seen in a Chest Clinic (1948–51)**

J. H. THOMAS, D. B. MORGAN, and T. W. DAVIES. *British Medical Journal* [*Brit. med. J.*] **2**, 1325–1329, Dec. 4, 1954. 6 refs.

Between 1948 and 1951 298 cases of primary pulmonary tuberculosis were seen at the Swansea Chest Clinic, which serves an area with a population of 230,000. The clinical features of these 298 cases, which included cases seen as contacts and in hospital as well as at the clinic, and the results of a follow-up investigation in July, 1953, are analysed in this paper. The youngest patient was 4 months of age and the oldest 28 years. In 57 cases the lesion was calcified and considered to be healed when the patient was first seen; in 192 (79·7%) of the remainder there was uneventful clinical and radiological healing. The recovery rate without complications was 83 to 90% in children under 12 years of age, 71% in children between 12 and 15 years, and 52% in patients of 16 to 19 years. Progressive primary tuberculosis or other forms of pulmonary tuberculosis were the commonest complications in patients over the age of 12, in contrast to persistent collapse and haematogenous spread in children under that age.

One-third of the 57 patients with a " radiologically healed " lung lesion had other symptoms of tuberculosis, including tuberculous meningitis in one and a tuberculous knee in one. These 57 cases were not followed up. Of the whole group of 298 patients 70% presented with definite symptoms, including erythema nodosum (18%), pleural effusion (6%), and a post-primary lesion (11%). Minor general symptoms were the commonest [but it is difficult to ascribe these specifically to the tuberculous infection].

Complications developed in 49 (16·4%) of the 298 cases in the series. In 44 patients there was at some stage radiological evidence of collapse, the right upper or right middle lobe being affected in 31; in 25 cases the lung aerated spontaneously within 2 years. Bronchiectasis developed in 7 of the 44 patients, being severe in 3. Resection was carried out in one of these and also in 4 cases in which collapse persisted without evidence of bronchiectasis.

There were 9 cases of miliary tuberculosis and 8 of tuberculous meningitis, in all of which the primary lesion was radiologically visible. Other cases of miliary or meningeal tuberculosis are mentioned [but the number is not stated and it is not clear whether and how often these two conditions occurred in the same patient]. In most of the cases the complication was the presenting feature. Progression of the pulmonary lesion was observed in 12 patients, all of them 14 or more years old. There was a satisfactory response to treatment in these cases, operation being performed in 4. Other pulmonary complications were seen in 10 patients, 2 of whom (a girl of 4 and a

youth of 18) were operated on. A boy of 7, who was considered unsuitable for pneumonectomy, died.

In the majority of cases treatment consisted in rest in bed at home for about 4 months; in addition, children were not allowed to attend school for a further 6 to 9 months. Streptomycin and PAS were not given as a routine, but were administered when there was progression of the parenchymatous component, bronchogenic spread, or blood-stream dissemination. Altogether 11 patients were subjected to a major intrathoracic operation. [The mortality in this group is not stated.]

John Lorber

884. **Tuberculous Pleural Effusions Treated by Prolonged Bed Rest**

P. A. EMERSON. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 261–273, Oct., 1954. 39 refs.

Follow-up over a period of 2 to 5 years showed that in 12 out of 40 cases of tuberculous pleural effusion further manifestations of tuberculosis occurred despite treatment with prolonged bed rest and a sanatorium regimen. All the patients were treated by the author in an R.A.F. hospital, there being 35 males and 4 females between 18 and 25 years of age and one male aged 30. Apart from 3 known cases of tuberculosis, all were apparently healthy at the time of onset. In every case the Mantoux test was positive to first or second strength P.P.D. In 32 cases the lung fields were clear on initial *x*-ray examination; in 8 others a parenchymal lesion was present. The diagnosis of pleural effusion was confirmed in each case by aspiration of clear, straw-coloured fluid containing lymphocytes. Tubercle bacilli were isolated from the fluid by culture or guinea-pig inoculation in 6 cases, and from the sputum or gastric washings in 7 cases. Of the remaining 27 cases, definite radiological evidence of tuberculous infiltration of the lung was present in a further 4, and histological evidence of tuberculosis was obtained on decortication in another. Thus in 18 (45%) of the 40 cases there was definite evidence of tuberculous infection.

Treatment was with strict bed rest for at least 3 months, followed by slowly increasing activity over a further 3 months. No chemotherapy was used, and fluid was removed only on account of pressure symptoms or failure of spontaneous absorption. In one case decortication was carried out 180 days after the onset of the effusion. The response to treatment was judged from the rate of fall of temperature and erythrocyte sedimentation rate and of disappearance of the pleural fluid as shown by serial radiographs of the chest.

After discharge from hospital all patients were referred to the out-patient care of their local chest clinic, and all 40 have been followed up by the author for at least 2 years (25 for 3 years, 7 for 4 years, and 2 for 5 years). Further manifestations of tuberculosis have developed as follows: (1) cervical adenitis, 1 case; (2) homolateral pleural effusion followed by pulmonary infiltration, 1 case; (3) contralateral effusion, 2 cases; and (4) pulmonary infiltration, 8 cases. These further manifestations appeared in 7 cases within one year and in 9 cases within 2 years of the onset of the illness. Of the 32 cases with initially clear lung fields, further manifestations of tuberculosis subsequently developed in 11, whereas of the 8 with parenchymal lesions, only one broke down.

The author does not agree with those who advocate the early aspiration of the pleural fluid in this type of case, the fluid clearing spontaneously and completely in the majority of his cases. He is disappointed with the results of bed rest alone in this series, and suggests that initial treatment with streptomycin and PAS or isoniazid might have prevented the high incidence of subsequent tuberculosis.

I. M. Librach

885. **Initial Tuberculous Pleuritis in the Finnish Armed Forces in 1939–1945. With Special Reference to Eventual Postpleuritic Tuberculosis.** [In English]

J. PÄTIÄLÄ. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] Suppl. 36, 1–57, 1954. 1 fig., bibliography.

886. **The Late Emergence of *M. tuberculosis* in Liquid Cultures of Pulmonary Lesions Resected from Humans**

G. L. HOBBY, O. AUERBACH, T. F. LENERT, M. J. SMALL, and J. V. COMER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 191–218, Aug., 1954. 24 refs.

At the Veterans Administration Hospital, East Orange, New Jersey, necrotic pulmonary lesions were cultured for *Mycobacterium tuberculosis*. The lung specimens were frozen immediately after they were removed, and stored in the frozen state until dissection. The dissected lesions were homogenized in an albumin medium, the suspension being centrifuged for 30 minutes and then washed three times with the same medium. Cultures from the deposit were incubated for as long as 9 months. *Myco. tuberculosis* was isolated from 21 out of 27 closed or healed lesions from 11 out of 15 patients, who had received chemotherapy for 4 to 12 months before operation. In 9 instances the organisms appeared only in subcultures after the fluid medium had been incubated for more than 83 days; one positive culture was obtained after 223 days. Only 10 of the lesions were capable of producing tuberculosis on direct inoculation into guinea-pigs, these being the lesions from which *Myco. tuberculosis* had been easily cultured. Positive cultures were readily obtained from the lesions of 4 controls who either had not received chemotherapy or had open cavities at the time of resection. All the strains of *Myco. tuberculosis* isolated were found to be virulent for guinea-pigs.

The significance of the findings is discussed. It is concluded that tubercle bacilli are capable of surviving in a dormant state in a healed or partly healed necrotic lesion, even after prolonged chemotherapy, and can be demonstrated by suitable methods of culture.

D. G. ff. Edward

887. **The Treatment of Tuberculous Cavities in the Apical Segment of the Lower Lobe**

J. RIMINGTON. *Tubercle* [*Tubercle (Lond.)*] **35**, 244–250, Oct., 1954. 7 refs.

See also Bacteriology, Abstract 855.

Venereal Diseases

888. **Tetracycline in the Treatment of Certain Venereal Diseases**
M. MARMELL and A. PRIGOT. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] 4, 1117–1121, Oct., 1954. 7 refs.

Tetracycline hydrochloride was given by mouth to 115 patients with gonorrhoea (68 of whom were adequately followed up), 2 with lymphogranuloma venereum, and 5 with chancroid at the Harlem Hospital, New York. Two dosages of tetracycline were used in the treatment of the patients with gonorrhoea—namely, 500 mg. 6-hourly to a total of 1·5 g. and 500 mg. followed at 6-hourly intervals by 250 mg. to a total of 1 g. Of the 50 patients followed up who had received the larger dosage, 49 were cured; of the 18 patients followed up who received the smaller dosage, 16 were cured. The patients with lymphogranuloma venereum and chancroid received 1 g. of tetracycline daily until the lesions were healed. Both of the patients with lymphogranuloma venereum responded favourably and the lesions healed after 10 to 11 g. had been given. There was a similar favourable response in all 5 cases of chancroid, the lesions healing after administration of 10 to 21 g.

No untoward side-reactions were noted in any of these cases. *R. R. Willcox*

889. **The Present Problem in the Control of Venereal Diseases.** (El problema de actualidad en el control de las enfermedades venéreas)
E. G. CLARK. *Boletín de la Oficina sanitaria panamericana* [*Bol. Ofic. sanit. pan-amer.*] 37, 154–155, Aug., 1954.

The author points out that the present mood of extreme optimism following the success of venereal disease control programmes recalls the events which followed the first World War, when a similar optimism was accompanied by a relaxation of control measures and a rise in the incidence of venereal disease consequently occurred.

In the United States the incidence of primary and secondary syphilis has fallen precipitately, but this fact should be interpreted with caution because a decline in case-finding activity is always followed by a decline in the apparent incidence. Further, discovery of a case of early latent syphilis signifies that a case of primary or secondary syphilis has been missed, and 3 latent cases are now found for every one of primary or secondary syphilis. Moreover, the incidence of early syphilis has recently risen in 9 States and 11 of the big cities, while the incidence of gonorrhoea in the U.S.A. is now higher than in any year before 1943, although below the peak reached in1947, and gonorrhoea is the second commonest notifiable infectious disease. In the opinion of the leading American medical organisations concerned with the problem, the programme for venereal disease control should be intensified in the coming years, being directed towards identifying and overcoming the foci of most resistance, and giving more attention to latent syphilis and gonorrhoea. It is emphasized that the cost of control measures does not fall in proportion to the reduction in the number of cases for, as the incidence decreases, so the cost of localizing each case rises. Thus motives of false optimism or misguided economy should not be allowed to vitiate a programme which has been, so far, brilliantly successful.

[This is a strong warning from an authoritative source.] *Eric Dunlop*

890. **Further Observations on Streptomycin Treatment of Gonococcal Infection.** (Ulteriori osservazioni sulla terapia streptomicinica nell'infezione gonococcica)
A. CHIARENZA. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] 95, 381–384, July–Aug., 1954.

The author reported 3 years ago that of a series of 421 patients with gonorrhoea who were treated with two doses of 250 mg. of streptomycin given intramuscularly, 419 were cured. He now reports that of a new series of 30 patients treated in the same way at the Venereological Clinic of the University of Catania, only 22 were cured with the above dosage, 3 requiring a total dose of 750 mg. and 5 being resistant to treatment. The 5 streptomycin-resistant patients included 2 of the 5 who had previously been treated with the drug and 3 of the remaining 25, none of whom had received streptomycin previously. Whereas in the former series gonococci had disappeared from the discharge within 2 hours of the first injection, it took 4 to 5 hours in the present series to eliminate them. Subjective symptoms disappeared rapidly in all cases. The resistant cases responded to treatment with penicillin and sulphonamides. *Ferdinand Hillman*

891. **Long-term Studies of Results of Penicillin Therapy in Early Syphilis**
J. K. SHAFER, L. J. USILTON, and E. V. PRICE. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] 10, 563–578, 1954. 4 figs., 2 refs.

The authors describe an investigation carried out by the Division of Venereal Disease of the U.S. Public Health Service to evaluate the long-term results of the treatment of syphilis with penicillin. At each of 11 treatment centres, beginning in 1945, a group of patients was selected for intensive post-treatment observation, the basis of selection being the probability that observation could be maintained in each case for at least 5 years. Out of 1,570 patients so selected during a 6-year period, 1,336 (85·1%) remained under observation, while 29,884 (89·4%) of the 33,441 examinations scheduled were carried out, an average of 19 per patient. Since the results of treatment in this group were almost identical

with those in a group of patients followed up by routine methods (42 to 64% complete) it is concluded that the outcome in patients who did not complete the full period of observation was the same as in those remaining under observation.

One series of 679 patients with secondary syphilis were treated with penicillin alone in a total dosage of 1·5 to 4·8 mega units (average 3·2 mega units), while another series of 292 patients with secondary syphilis were treated with arsenoxide (maximum total dosage 300 mg.) and bismuth (total dosage 600 mg.) in addition to penicillin (total dosage 1·2 to 4·8 mega units). The cumulative re-treatment rate for 554 of the patients given penicillin alone was 13·7% at 2 years and 16·3% for 157 patients at 5 years, while after treatment with penicillin, arsenic, and bismuth the rate was 16% at 2 years for 269 patients and 17·4% at 5 years for 159 patients. It is concluded that the use of arsenic and bismuth does not enhance the effect of penicillin given alone. The results of treatment of early syphilis with penicillin were clearly superior to those obtained with arsenic and bismuth. A minimum of 4·8 mega units of penicillin is recommended in the treatment of early syphilis.

Eric Dunlop

892. **Treatment of Early Infectious Syphilis with N:N′-Dibenzylethylenediamine Dipenicillin G. A Second Report**

J. K. SHAFER and C. A. SMITH. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **10**, 619–626, 1954. 2 figs., 3 refs.

The authors report the results of the treatment of 196 cases of dark-ground-positive early syphilis with a single injection of 2·5 mega units of N:N′-dibenzylethylenediamine di(benzylpenicillin) (" bicillin "; benzathine penicillin) at three treatment centres cooperating with the Division of Venereal Disease of the U.S. Public Health Service. Follow-up was short, all but 26 cases being observed for less than 18 months after treatment. In cases of secondary syphilis the cumulative re-treatment rate after 21 months was 4·1% with benzathine penicillin as against 14·2% after a single injection of 2·4 mega units of procaine benzylpenicillin with 2% aluminium monostearate (P.A.M.), and 5·1% after a single injection of 4·8 mega units of P.A.M. The authors conclude that a single injection of 2·5 mega units of benzathine penicillin is as effective as one of 4·7 mega units of P.A.M.

Eric Dunlop

893. **Transfusion Syphilis and its Importance in Blood-bank Organization.** (Die Transfusionslues und ihre Bedeutung für das Blutspendewesen)

G. AMMON. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **17**, 216–220, Oct. 1, 1954. 1 fig., 40 refs.

In his work at the Berlin Blood Transfusion Service the author has encountered, among a total of some 16,000 blood donors examined in the last 3 years, 63 whose blood gave a strong positive reaction for syphilis. This represents an incidence of 0·4%. (More recently, owing to the influx of refugees from eastern Germany and their occasional use as donors, this figure has probably risen to 2 or 3%.) It was noted in one case that as early as 7 days after the primary syphilitic infection of a donor his blood infected the recipient, the former developing a chancre 20 days later and the latter *syphilis d'emblée* 4½ weeks later.

The author then describes his personal investigation of 88 cases of transfusion syphilis, of which 30% were due to the use of " occasional " donors (usually relatives); in 28% the donor was symptomless, the disease being in the incubating or latent stage, and in 9% technical faults were responsible, in 4 of the cases syphilis actually being transmitted from the recipient to the donor. Transfusion syphilis is a *syphilis d'emblée* without primary lesions, and its incubation period is from 1 to 3½ months. The affected patient should be informed of the accident at once and treated even before it is certain that the disease has been transmitted. When fresh blood is used absolute prevention is impossible, but in all cases a clinical examination of the donor, including the genitalia, should be made. Highly sensitive tests like the Chediak reaction or the cardiolipin flocculation test may reveal the presence of latent syphilis. In the author's opinion the addition of oxide of arsenic to fresh blood does not solve the problem, and moreover has been shown to produce haemolysis on storage; if this method is adopted it should be carried out 10 minutes before the blood is used. Perhaps the safest method is to store the blood for 72 hours at a temperature between 2° and 4° C.

Ferdinand Hillman

894. **Factors Leading to Development of Late Manifestations of Syphilis**

E. W. THOMAS, J. K. SHAFER, M. R. ZWALLY, and E. V. PRICE. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 531–553, Nov., 1954. 3 figs., 4 refs.

895. **Abacterial Urethritis: a Report of Eight Cases with Isolation of the Pleuropneumonia-like Organism**

W. J. HOLLIS. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 671–676, Oct., 1954. 8 refs.

At the U.S. Air Force Hospital, Barksdale, Louisiana, over a 27-month period, 179 cases of gonococcal urethritis were encountered, as compared with 17 cases of urethritis due to pleuropneumonia-like organisms (P.P.L.O.), 6 cases of non-venereal urethritis of unknown origin, and one case of bacterial urethritis. Of the 17 cases due to P.P.L.O., 8 for whom sufficient information was available are described in detail. Three of these cases occurred soon after the treatment of gonorrhoea and one case 5 months after such treatment. A fifth patient admitted sexual contact 2 months previously, but the remaining 3 denied such contact. The author claims that these observations suggest a venereal transmission of the disorder. Of 4 of the patients treated with streptomycin alone (in doses of 5 to 9 g. for 5 to 9 days), all showed a good response. The other 4 cases were treated with a combination of streptomycin and sulphadiazine and also showed good response, and it is suggested that this was due mainly to the streptomycin and not to the sulphadiazine.

R. R. Willcox

Tropical Medicine

896. **Isolation of the Virus as a Diagnostic Procedure for Yellow Fever in West Africa**
F. N. MACNAMARA. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] 11, 391–401, 1954. 2 figs., 9 refs.

The diagnosis of yellow fever by demonstrating a rise in the titre of antibodies in the patient's serum is impossible if protective vaccination is carried out in the interval between taking the blood samples, and as this is increasingly likely to occur during epidemics, the alternative method of diagnosis by isolation of the virus from the blood is in many ways preferable.

During four epidemics of yellow fever in West Africa between 1946 and 1952 the virus was isolated on 88 occasions from 73 patients by the injection of undiluted serum intracerebrally into Swiss mice. The mice were observed for sickness, paralysis, and death for 30 days before being discarded. Passage was accomplished with mouse-brain material in non-immune human serum with saline, and the specificity of the virus confirmed by neutralization tests with specific immune serum.

The greater speed with which diagnosis can be made by isolation of the virus compared with the serological method is of importance—for routine serological tests two samples of blood are required at an interval of 2 or 3 weeks, and it may be a month before the diagnosis is confirmed—and it is considered that the former method is a reliable practical procedure in West Africa if attempted early in the illness. If the case is a severe one the virus is present in the blood for 6 or more days. The mice may be expected to become sick usually within 8 to 10 days of inoculation, giving strong presumptive evidence of the disease. A specificity test should give confirmatory evidence in another 9 to 10 days. *R. R. Willcox*

897. **The Chemotherapy of Leprosy. Late Results of Treatment with Sulphone, and with Thiosemicarbazone**
J. LOWE. *Lancet* [*Lancet*] 2, 1065–1068, Nov. 20, 1954. 16 refs.

This paper describes the results of the treatment of leprosy with sulphones and thiosemicarbazones in East Nigeria, as observed in some cases as long as 8 years after its initiation. In March, 1954, 117 cases were reviewed in which treatment with sulphone (diaminodiphenylsulphone) had been started between 6 and 8 years previously. Of the 109 lepromatous cases, in 97 the disease had been arrested and in 12 there was clinical arrest of the disease, although smears still showed a few bacilli; of the 8 tuberculoid cases there had been arrest of the disease in all. In none of these 117 cases had sulphone therapy failed to produce definitive and progressive improvement leading eventually to clinical inactivity, and although in many cases there had been long periods during which progress was inappreciable, improvement had never been followed by deterioration, so that it would seem that drug resistance does not develop with the usual dosage of sulphones.

During the period 1946–54 252 patients treated exclusively with sulphone were rendered fit for discharge. Of the 162 patients with the lepromatous type, 139 had been re-examined at least once since discharge, slight evidence of relapse being found in 15 (11%); in 2 of these cases slight neuritis was present which responded quickly to further treatment; in the others smears contained a few bacilli which disappeared without further treatment. Of the 90 patients with tuberculoid leprosy, 69 had been re-examined, among whom 8 showed clinical reactivation. In 7 cases the relapse occurred in 3 to 12 months after treatment, and in the eighth case after 28 months; in 6 of the 8 the patient had received less than the usual period of treatment, and in view of this a minimum of 18 months' treatment is recommended for tuberculoid cases.

Treatment with thiosemicarbazone in the form of thiacetazone (*p*-acetylaminobenzaldehyde thiosemicarbazone) was started in October, 1950, 273 patients having since been treated for periods up to 38 months. The earlier promise of this treatment has not been entirely fulfilled, and three serious types of toxic effect have been seen—acute agranulocytosis (5 cases), severe acute toxic anaemia (6 cases), and severe hepatitis (3 cases). Two deaths occurred probably as a result of the treatment, and 3 other patients died from fulminating gastro-enteritis possibly aggravated by it. Compared with the sulphones, thiacetazone is more expensive and more troublesome to administer, and it is liable to lose its therapeutic action. It is therefore recommended that its use should be confined to: (*a*) patients who have become allergic to sulphones; (*b*) patients who suffer serious toxic effects (such as psychosis) from sulphones; and (*c*) cases in which sulphone administration is difficult for any other reason. When the patient has improved sufficiently, sulphone treatment should be resumed if possible. It is emphasized that the two drugs should not be given together; the toxic effects are increased, and the clinical response is no better than with either drug alone.

[This is an important paper showing the major revolution in the treatment of leprosy which has occurred during recent years owing to the introduction of sulphone treatment. In most cases, in Africa at any rate, leprosy can now be cured, and this at a cost within the means of the public health services.] *F. Hawking*

898. **Studies in Human Strongyloidiasis. II. A Comparison of the Efficiency of Diagnosis by Examination of Feces and Duodenal Fluid**
C. A. JONES and S. H. ABADIE. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] 24, 1154–1158, Oct., 1954. 1 fig., 7 refs.

Nutrition and Metabolism

899. **High Protein Feeding in the Elderly**
LORD AMULREE, P. FREEDMAN, D. GEFFEN, and S. TRACY. *Medical Officer* [*Med. Offr*] **92**, 227, Oct. 29, 1954.

Experience having shown that elderly people for various reasons often consume a diet which is deficient in first-class protein, the diet of a group of elderly patients at University College Hospital, London, and of a number of similar subjects attending a local clinic was supplemented with 26 g. daily of a highly-concentrated milk derivative. The results in the clinic patients were assessed from the statements and impressions of the patients themselves, without a control series. At the hospital, where 16 patients received the dietary supplement and 16 served as controls, the results were assessed from clinical observations and from blood pressure and the haemoglobin, blood urea, and serum protein levels. No significant objective or subjective improvement was recorded in either the hospital or clinic patients. A slight change in the serum protein level was observed in 3 of the former, but in neither group was there any increase in the blood urea level or blood pressure. The preparation was generally well tolerated. The authors conclude that for persons subsisting on suboptimal quantities of first-class protein a high-protein preparation such as that used in this investigation is a suitable dietary supplement.

J. N. Agate

900. **Human Nutrition and the Sophistication of Foods and Feeding Habits. Some Observations, Implications, and Speculations**
B. S. PLATT. *British Medical Journal* [*Brit. med. J.*] 1, 179–185, Jan. 22, 1955. Bibliography.

901. **Nutritional Intake of Children. II. Calcium, Phosphorus and Iron**
V. A. BEAL. *Journal of Nutrition* [*J. Nutr.*] **53**, 499–510, Aug. 10, 1954. 4 figs., 11 refs.

Data have been presented from 795 nutrition histories on 58 children in the first 5 years of life. Calcium, phosphorus, and iron intakes have been computed in terms of quartiles and maximum and minimum levels observed. In addition, some of the individual patterns of calcium intake have been shown.

Intake of calcium rises rapidly in the first 6 months, less rapidly between 6 and 9 months, then decreases to a lower level between 2 and 3 years, when the median calcium level is 0·75 g. and the median milk intake is 16 ounces (454 ml.). This is followed by an increase in milk and in total calcium. There is a sex difference in calcium intake between 6 and 15 months, with the boys reaching a higher level than the girls and maintaining that level for a longer period of time.

Phosphorus intake increases during the first year, then shows a pattern intermediate between the stationary intake of protein and the markedly decreased intake of calcium in the early pre-school years, increasing again between 3 and 4 years.

The sharp rise of iron intake during the first year, due primarily to the high iron content of commercially prepared infant cereals, is followed by a decrease as these foods are replaced in the diet. After 3 years, levels of iron intake increase, but from 2 and 1½ years to 5 years more than 75% of the intakes remain below the Recommended Allowance of the National Research Council.—[Author's summary.]

902. **The Diets of Young Children**
E. R. BRANSBY and J. E. FOTHERGILL. *British Journal of Nutrition* [*Brit. J. Nutr.*] **8**, 195–204, 1954. 11 refs.

During April, 1951, a survey was carried out in 10 different localities in England of the diet of children in the age groups 6 to 12 months, and 1, 2, 3, and 4 years, each group containing 150 children. After eliminating those children who were not fully weaned or who were not taking all their meals at home, those who could not be interviewed, and those whose mothers would not or could not participate, records were obtained for 461 children. The diet consumed by each child was recorded by the mother by weight, volume, and standardized measures. Other information included weekly income of the head of the family, the size of the family, and whether or not the mother went out to work.

The average consumption of various foods and the average intake of calories and nutrients in each age group are recorded. In the detailed information given a few points are of special interest. There was considerable variation between individuals in each age group [an observation made and commented on by many other workers]. Comparison with the only similar investigation, which was carried out before the war mainly among middle-class children by Widdowson (*Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), 1947, No. 257), shows a similar intake of foods and of calories and of nutrients, with a few striking exceptions. Thus the consumption of milk was somewhat less in 1951, as was the intake of calcium, while the intakes of vitamin A and of ascorbic acid were substantially less. [The authors do not comment on these findings, some of which are rather surprising.]

By assessing the intake as low, high, or medium for each nutrient and for each child, depending on whether the amount was in the lowest, highest, or intermediate quartile, the authors found interesting variations in different groups. Thus the intake of calories and nutrients was higher in boys than in girls, and higher in children whose mothers went out to work than in those whose mothers did not. There was also a higher intake of calories and nutrients by children belonging to large families and families in low-income groups. [These results, as the authors suggest, are most surprising. The

surveys of the Ministry of Food have shown decreased consumption in children of larger or poorer families, and it is also known that body weight and other criteria of nutritional status are inferior in these children.]

John Yudkin

903. **Mode of Action of Vitamin D. Histochemical Study of Rachitic Epiphyseal Cartilage during Healing in Albino Rat**

V. RAMALINGASWAMI, S. SRIRAMACHARI, P. K. DIKSHIT, P. G. TULPULE, and V. N. PATWARDHAN. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **8**, 509–516, Aug., 1954. 14 figs., 24 refs.

The changes observed in the epiphyseal cartilage of the rachitic rat after administration of calciferol (vitamin D) are described in this paper from the Indian Council of Medical Research, Coonoor. It was found that administration of calciferol to young rats in which rickets had been induced led to an increase in glycogen in the proliferative zone of the cartilage before calcification, followed by a reduction as calcification began. A reduction in nucleoprotein-like material, an increased periodic-acid–leucofuchsin reaction, and a reduction in alkaline-phosphatase activity were noted in the matrix of rachitic cartilage during calcification. Similar changes were observed when calcification was induced by a citric-acid–sodium-citrate mixture. It is suggested that the defect of calcification in the rachitic animal may be due to a failure of glycogen metabolism before citrate formation.

F. W. Chattaway

904. **Ammonia Metabolism in Man**

W. V. MCDERMOTT, R. D. ADAMS, and A. G. RIDDELL. *Annals of Surgery* [*Ann. Surg.*] **140**, 539–556, Oct., 1954. 10 figs., 40 refs.

In this paper from Harvard Medical School the present concepts of normal ammonia metabolism are reviewed and observations on man are reported which confirm others on experimental animals, namely, that portal venous blood contains much more ammonia than arterial or mixed venous blood, and that renal venous blood contains more ammonia than renal arterial blood.

Case reports are then given of 3 patients with hepatic cirrhosis without portacaval shunts, 4 with cirrhosis and a portacaval shunt, and 2 with a portacaval shunt but without liver disease. In all these three types of case episodic stupor, with neurological signs and electroencephalographic abnormality, was associated with the administration of a high-protein diet, with giving urea or ammonium resin, or with gastrointestinal bleeding. The blood ammonia level was raised during such episodes, but some cerebral dysfunction might persist for a time after the ammonia content had fallen somewhat, though not to normal levels. In the treatment of such episodes, protein restriction is stated to be of first importance, and the authors suggest that the control of gastrointestinal haemorrhage, the use of sulphonamides to inhibit the growth of urease-producing organisms, and the giving of sodium resins to take up intestinal ammonia may all be of value in reducing the amount of ammonia entering the portal vein.

D. A. K. Black

905. **Influence of the Gastric Juice on Tissue Metabolism**

G. DOMINICI, G. OLIVA, and C. TRAMONTANA. *Lancet* [*Lancet*] **2**, 1105–1106, Nov. 27, 1954. 1 fig., 8 refs.

In experiments carried out at the Medical Clinic of the University of Perugia gastric juice withdrawn by intubation from a healthy subject was centrifuged to remove gross particles, brought to *p*H 7·5 by the addition of sodium bicarbonate and sodium carbonate, and then filtered. Of the filtered gastric juice so prepared, 5 ml. was injected intramuscularly into normal subjects and patients with various types of anaemia and achlorhydria, in all of whom it caused a lowering of the blood sugar, serum iron, and serum amino-acid levels, the effect being greatest 4 to 6 hours after the injection. Similarly prepared gastric juice from patients with anaemia, with and without achlorhydria, yielded similar responses with the exception of gastric juice from cases of so-called achlorhydric iron-deficiency anaemia. On the basis of these results the authors suggest that the primary fault in achlorhydric iron-deficiency anaemia is not a failure of absorption of iron but a fault of tissue metabolism, particularly of oxidation. This condition, which they term " dysendoatmia ", is in their opinion due to deficiency of a factor present in normal gastric juice which is destroyed by heating the preparation in a water bath for one hour at 60° C., and they claim that it can be cured by making good the deficiency. An illustrative case is reported. The authors also state that the oral complications of antibiotic therapy respond to the parental injection of " normal gastric juice " [presumably gastric juice prepared as described above, which cannot really be considered normal].

R. E. Tunbridge

906. **Utilization and Intestinal Excretion of Calcium in Man**

M. BLAU, H. SPENCER, J. SWERNOV, and D. LASZLO. *Science* [*Science*] **120**, 1029–1031, Dec. 17, 1954. 1 fig., 2 refs.

METABOLIC DISORDERS

907. **Sodium Salicylate and Probenecid in the Treatment of Chronic Gout. Assessment of their Relative Effects in Lowering Serum Uric Acid Levels**

F. G. W. MARSON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 233–245, Sept., 1954. 8 figs., 24 refs.

The occurrence of the symptoms of chronic gout is closely related to the presence of a high uric acid content in the serum and tissue fluids, and the therapeutic value of increasing the excretion of uric acid has long been known. The author has compared the effect of sodium salicylate and probenicid in lowering the serum uric acid level in 21 cases of chronic gout over a period of 45 months at the General Hospital, Birmingham. He draws attention to the fact that the effect of both drugs is at a maximum in the first few days of administration, the initial degree of response not being maintained during prolonged therapy. Of the two drugs, salicylates have the more lasting and more marked effect on the serum

uric acid level, 6·5 g. of sodium salicylate having approximately double the uricosuric effect of 2 g. of probenicid. Adequate treatment with either drug will not abolish all acute episodes. Toxic effects were observed with both drugs and some patients could not tolerate either in therapeutic doses.

[Many practical points are mentioned in the article, which is profusely illustrated and should be read in the original by all interested in the treatment of chronic gout.]

R. E. Tunbridge

908. **Renal Clearance of Endogenous Porphobilinogen in Man**

A. GOLDBERG. *Lancet* [*Lancet*] 2, 1095–1097, Nov. 27, 1954. 10 refs.

Using a spectrophotometric method the author, at University College Hospital, London, determined the porphobilinogen clearance in 4 cases of porphyria, 2 in acute attacks, one in remission, and one during a latent phase. The results were compared with the creatinine and urea clearances, and in one case with the inulin clearance. The effect of posture on the clearance rates was determined in one case, the results of all tests being higher when the patient was in a reclining position—findings which are not in accordance with those of other workers. The author suggests that the mechanism of excretion of porphobilinogen is closely related to that of creatinine in view of the close correlation between their clearance rates. He considers that in acute porphyria porphobilinogen is formed in the liver and is excreted by glomerular filtration without appreciable tubular reabsorption. [Further work is needed to confirm the hypothesis.]

R. E. Tunbridge

909. **Porphyria. A Clinical and Neuropathologic Report**

G. A. SCHWARZ and J. A. L. MOULTON. *Archives of Internal Medicine* [*Arch. intern. Med.*] 94, 221–247, Aug., 1954. 14 figs., bibliography.

The clinical features in 3 cases of acute porphyria and the neuropathological findings in 2 of them are described in this paper from the University of Pennsylvania. The patients were women (2 being negro sisters) aged 17, 20, and 24 respectively. The illness began with abdominal pain which was not relieved by appendicectomy and the cause of which was not found at laparotomy. At varying periods after operation neurological symptoms, such as paralysis, muscle wasting, and sensory defects, developed which were complicated by convulsions, confusion, hallucinations, and delirium. All 3 patients died.

Necropsy was performed in 2 cases, and the neuropathological features are described as those of a diffuse toxic meningopolioencephalomyelitis. There was widespread degeneration of neurones in the cerebral cortex, brain stem, autonomic ganglia, and spinal cord, the anterior horns of the cervical and lumbar enlargements of the cord being most affected. In the leptomeninges and within the central nervous system there was perivascular infiltration of plasma cells and lymphocytes, and in some places perivascular haemorrhage was observed. There was very little evidence of damage to myelinated fibres.

The authors briefly discuss the metabolic aspects of porphyria, and stress the difficulty of diagnosing acute or intermittent porphyria before the neuropsychiatric symptoms appear, these symptoms varying considerably from case to case. They were able to find reports of only 4 cases of this type of porphyria in negroes.

A review of the pathological findings in 47 reported cases showed that the neuronal and vascular lesions observed in the authors' cases commonly involved the spinal cord, brain stem, cerebellum, and cerebrum, and that a multiple neuritis was often present. It was noted that the individual lesions and their distribution were in no way peculiar to porphyria, and it is suggested that the damage to the nervous system is the result of the direct cellular action of an unknown toxic agent.

Charles Rolland

910. **Symptomatic Uroporphyrinuria**

T. K. WITH and H. C. A. PETERSEN. *Lancet* [*Lancet*] 2, 1148–1151, Dec. 4, 1954. 10 refs.

At Rigshospitalet, Copenhagen, the authors estimated the urinary excretion of porphyrins in a series of 250 patients suffering from various diseases. The methods, which are described in detail, consisted in estimating the total porphyrin and the coproporphyrin present in the urine, the difference between these two values giving the amount of non-coproporphyrin porphyrin (NCP) in the urine. When NCP was found in appreciable quantities lutidine chromatography was used to differentiate between the various carboxyl porphyrins.

NCP was found in amounts varying between 50 and 500 μg. in the 24-hour urinary excretion of 16 patients, most of whom were suffering from serious and potentially fatal diseases. In many cases NCP appeared in the urine on one day only, and the amount excreted was much less than in porphyria; the coproporphyrin excretion was quantitatively normal in these cases. The authors conclude that several different porphyrins may be found in the urine of patients suffering from a variety of disorders, and that a moderate degree of uroporphyrinuria is not necessarily evidence of an inborn error of metabolism.

Charles Rolland

911. **Agammaglobulinaemia. A Congenital Defect**

N. H. MARTIN. *Lancet* [*Lancet*] 2, 1094–1095, Nov. 27, 1954. 1 fig., 12 refs.

The author describes the results of quantitative analysis by the Tiselius technique of the serum protein pattern in 4 premature infants at St. George's Hospital, London. In one infant weighing 22 oz. (623 g.) at birth there was complete absence of γ globulin, while in a second infant weighing 21 oz. (595 g.) the γ-globulin level was less than 0·1 g. per 100 ml. In the other 2 infants weighing 31 oz. (879 g.) and 34 oz. (964 g.) respectively, no deficiency of γ globulin was demonstrated.

The author draws attention to the similarity of the serum protein content in the 2 smaller and more premature infants to that found in 2 cases of agammaglobulinaemia, and suggests that this condition may be due to persistence of the early foetal serum protein pattern.

H. G. Farquhar

Gastroenterology

912. **The Gastroesophageal Vestibule. Its Normal Function and Its Role in Cardiospasm and Gastroesophageal Reflux**

F. J. INGELFINGER, P. KRAMER, and G. C. SANCHEZ. *American Journal of Medical Sciences* [*Amer. J. med. Sci.*] **228**, 417–425, Oct., 1954. 6 figs., 25 refs.

One of the difficulties arising in the study of the distal oesophagus and the gastro-oesophageal junction and their disorders is that in some cases what appears anatomically to be the lower end of the oesophagus is lined with gastric mucosa. The authors have attempted to define the extent of the oesophagus by studying its motor function on swallowing, measuring the intraluminal pressure by means of open-tipped catheters placed in position under *x*-ray control. In this way three parts can be identified: (1) the body of the oesophagus, extending from the pharynx to the inferior sphincter, which is an inconstant constriction about 3 cm. above the gastro-oesophageal junction; (2) the terminal few centimetres of the body, constituting the ampulla [a term misapplied by some authors to the third part]; and (3) the vestibule, or terminal part of the oesophagus below the inferior sphincter. Graphic records show that in normal subjects the wave of peristaltic pressure slows down in the ampulla and is not propagated into the vestibule at all, while other evidence is cited which suggests that the motility and tone of the vestibule are characteristic and independent.

In achalasia the vestibule is permanently contracted and the body of the oesophagus shows no normal tone or peristalsis. When methacholine was given to 3 patients with achalasia, radiological observation showed that in 2 cases the body of the oesophagus contracted, whereas the vestibule appeared to relax. [The alternative explanation of the changes as seen on the *x*-ray screen is that a small hiatal hernia forms.] When 2 healthy male subjects (aged 63 and 71) were given 35 mg. of methantheline intravenously, in both cases the body of the oesophagus lost its tone, whereas the vestibule contracted. Cholinergic and anticholinergic stimuli thus seem to affect body and vestibule in opposite directions, and it is suggested that just as cardiospasm is due to achalasia of the vestibule, vestibular chalasia, or failure to remain contracted between swallows, may underlie some forms of gastro-oesophageal reflux. [Other and more plausible hypotheses are not discussed.]

Denys Jennings

913. **The Adverse Effects of Belladonna Alkaloids in Benign Pyloric Obstruction. An Experimental Study**

P. KRAMER. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 600–605, Oct. 7, 1954. 1 fig., 14 refs.

The author, writing from Boston University School of Medicine, points out that the alkaloids of belladonna are frequently prescribed in the medical treatment of chronic peptic ulcer, gastric retention, and benign pyloric stenosis on the ground that they relax the spasm of the pylorus. In the author's view this reasoning is faulty, in that emptying of the stomach is probably determined more by the tone of the gastric musculature and the amount of peristalsis than by the state of the sphincter and the size of the pyloric outlet.

In order to throw further light on this point 15 patients with duodenal ulcer and present or recent clinical or radiological evidence of pyloric obstruction (Group A) were compared with a group of control cases with no such obstruction (Group B). Group A were divided into four subgroups consisting of 8 patients in whom symptomatic pyloric obstruction had recently been treated by gastric suction, 3 with untreated symptomatic obstruction, one with symptomless obstruction, and 3 with a past history of pyloric obstruction who were free of symptoms at the time of investigation. The control group consisted of 3 women with no disease, 4 patients with functional gastrointestinal disorders, and 7 with healed or active peptic ulcer but without radiological or symptomatic evidence of pyloric obstruction. After a short period of observation without medication all the subjects were given either 0·6 mg. of atropine subcutaneously, 0·5 mg. of "bellafoline" (a preparation containing all the laevorotary alkaloids of belladonna leaf) subcutaneously, or 12 to 15 drops of the tincture of belladonna orally. The rate of the passage of a barium meal out of the stomach was assessed radiologically before and after administration of the alkaloids.

In all cases, except in 3 of the normal control subjects, the effect of the alkaloids was to prolong the emptying time of the stomach. In 9 of the 15 patients retention up to 5 hours occurred, and in 4 retention was complete even after 5 hours. It was notable that prolongation was most marked in the patients with pyloric obstruction. It is concluded therefore that belladonna alkaloids should be used cautiously in cases of pyloric obstruction, and discontinued entirely if the patient fails to improve.

T. D. Kellock

914. **Gastric Volvulus**

C. GOTTLIEB, D. LEFFERTS, and S. L. BERANBAUM. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 609–638, Oct., 1954. 25 figs., 38 refs.

This paper from the University Hospital, New York, is in three parts, of which the first is a review of the literature and of the various elaborate aetiological and topographical classifications of gastric volvulus which have been proposed. The authors conclude that the condition may be secondary to a lesion in the stomach or, more frequently, in the neighbouring organs (the most important being congenital elongation of the gastrohepatic or gastrocolic omentum, or of both), or due to no demonstrable cause (idiopathic volvulus).

Part II contains brief reports of 9 cases of the idiopathic type which were diagnosed radiologically. Only in one of these was an operation performed, and then it was at another hospital, where nothing abnormal was found. [No follow-up details are reported, and it is far from clear that the vague upper abdominal symptoms in these cases were related to the volvulus.]

Part III contains brief reports of 11 cases in which gastric volvulus was associated with some lesion of the stomach or other organs. In 5 cases there was a hiatal hernia or eventration of the diaphragm. In another case there was a large inoperable carcinoma of the pancreas as well as an eventration, while in a second case of carcinoma of the pancreas operation confirmed that rotation of the stomach was due to the large mass. Four other cases were associated with a peptic ulcer or diverticulitis; one of these came to necropsy, when the stomach was found to be normal in position and it was assumed that the volvulus had reduced itself.

[This series of 20 cases was collected over an unstated period of time and no indication of the incidence of gastric volvulus is given. It contains no example of the acute type with the classic triad of intense pain during retching, inability to vomit, and inability to swallow a stomach tube.] *Denys Jennings*

915. **Choleretic Action of Cortisone**

P. R. PATTERSON, J. F. DINGMAN, H. SHWACHMAN, and G. W. THORN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 502–508, Sept. 23, 1954. 2 figs., 23 refs.

A fall in the serum bilirubin level in patients suffering from liver disease when treated with either ACTH or cortisone has been recorded by a number of observers. The present investigation, which is reported from the Children's Medical Center and Peter Bent Brigham Hospital, Boston, was designed to determine whether cortisone caused an increased outflow of bile from the liver and thus lowered the concentration of bilirubin in the serum.

In 6 normal adults, 3 adult patients, and 6 child patients duodenal aspiration was performed under fluoroscopic control and the duodenal fluid collected at 15-minute intervals for 5 to 7 hours. The volume, colour, and bilirubin concentration were estimated, as well as the chloride, trypsin, amylase, and lipase content. To the normal subjects, after a preliminary period of collection of juice for 1 to 2 hours, 100 mg. of cortisone was given intravenously, when a rise in duodenal bilirubin concentration was found to occur during the first and second hours after injection. Of 7 patients similarly investigated, an increase in bilirubin output was recorded in 5. The volume of the bile was also increased, and this persisted for 3 or 4 hours, in contrast to the action of sodium dehydrocholic acid, which caused an increased flow for 30 to 45 minutes only.

The authors also observed that cortisone caused increased pancreatic enzyme activity in the duodenal fluid in patients with low initial values [but the figures given for the 2 cases on which this conclusion is based are not impressive]. *Thomas Hunt*

916. **Nutrition Liver Disease Due to Impaired Absorption.** [In English]

A. ARENDS, H. O. NIEWEG, and J. ENGELHARDT. *Acta medica Scandinavica* [*Acta med. scand.*] **150**, 163–168, Oct. 30, 1954. 13 figs., 29 refs.

The authors, from the University of Groningen, describe 11 cases of disease of the liver in which one of the following conditions was also present: ulcerative colitis, virus diarrhoea, failure of fat absorption as the result of resection of the small intestine, fibrocystic disease of the pancreas, coeliac disease, non-tropical sprue, and Whipple's disease. Steatorrhoea was present during life in 9 of these patients.

After reviewing the clinical features of these 11 cases and the findings at liver biopsy and at necropsy (fatty infiltration, fatty infiltration with fibrosis, diffuse fibrosis, acute necrosis, and post-necrotic scarring), the authors express the view that impaired absorption, which was the common feature in the different forms of intestinal disturbance, was the primary cause of the liver disease, a deficiency of lipotropic factors and sulphur-containing amino-acids being probably involved in the "nutritional failure" in such cases. They point out, in support of this view, that malnutrition can cause liver disease in man—as seen in kwashiorkor—and that liver disease has been induced in experimental animals by an inadequate diet. *Joseph Parness*

917. **The Place of ACTH and Cortisone in the Treatment of Chronic Hepatitis and Cirrhosis.** (La place de l'A.C.T.H. et de la cortisone dans le traitement des hépatites prolongées et des cirrhoses)

J. LEBON and G. GELIN. *Annales de médecine* [*Ann. Méd.*] **55**, 421–466, 1954. 10 figs., bibliography.

The authors report from the Hôpital Civil, Oran, Algeria, the results in 16 cases of liver disease treated with cortisone or ACTH (corticotrophin).

Of these patients, 6 had had viral hepatitis for at least one month and had not responded to conventional therapy. In each case the response to administration of the hormone was favourable, resulting in the diminution of jaundice, good diuresis, improved appetite, relief from itching, and, histologically, cell regeneration as confirmed by liver biopsy. The seventh patient, who suffered from severe hepatitis and was thought to be in a state of precoma, made an uneventful recovery when given cortisone. The remaining 9 patients had hepatic cirrhosis and included 2 cases of haemochromatosis, 5 of alcoholic cirrhosis, and 2 of doubtful aetiology. Appetite and well-being increased on treatment with the hormones, and a good diuresis almost invariably resulted. Hyperglycaemia was the only untoward complication attributable to the treatment. The relevant literature is extensively reviewed.

[It is difficult to assess the results of treatment in any liver disease without reference to a control series; in some of the present cases improvement may have been due to other factors associated with treatment in hospital. Nevertheless, the consistency with which jaundice decreased and urinary output increased in response to hormone therapy is impressive.] *P. C. Reynell*

Cardiovascular System

918. Blood Volume in Congestive Heart Failure as Determined with Iodinated Human Serum Albumin
E. KAPLAN, R. C. PUESTOW, L. A. BAKER, and S. KRUGER. *American Heart Journal* [*Amer. Heart J.*] **47**, 824–838, June, 1954. 39 refs.

Blood volume was determined in 32 cases of congestive heart failure. Repeat determination was made in 25 of the patients after treatment leading to compensation. Human serum albumin labeled with I^{131} was used in making these studies. Blood volume was elevated above normal in those cases studied. Total packed red cell volume was more markedly elevated than plasma volume.

In response to therapy the plasma component was more labile and decreased more rapidly than the cellular component. Hematocrit increased with therapy. During recovery from congestive heart failure the rate of apparent destruction of erythrocytes exceeded, in some instances, the expected calculated rate of destruction.—[Authors' summary.]

919. The Mechanics of Pulmonary Ventilation in Patients with Heart Disease
C. C. BROWN, D. L. FRY, and R. V. EBERT. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 438–446, Oct., 1954. 5 figs., 27 refs.

The authors have carried out a study at the University of Minnesota Medical School, Minneapolis, of the mechanics of ventilation, with particular reference to the cause of dyspnoea in patients with heart disease. Their method was based on the theory that the intrathoracic pressure at any time during breathing represents the sum of (1) the retractive forces of the lungs, (2) the pressure required to overcome tissue friction of the lung, and (3) the pressure gradient required to produce a flow of air through the bronchial tree. Intrathoracic pressure was measured by means of a balloon in the oesophagus, the difference between this pressure and that in the mouth being recorded by a differential strain gauge. The breathing was interrupted suddenly at any point by either a hand-operated three-way respiratory valve or an electrically operated solenoid valve. A spirometer tracing of the changes in lung volume was made. To differentiate between the pressure required to overcome tissue friction of the lung and the pressure gradient required to maintain the flow of gas through the bronchi it was necessary to make the subjects breathe two gases with different physical properties but about equal kinematic viscosity; those chosen were air and a mixture of oxygen (20%) and argon (80%). The increase in lung volume was plotted against the static intrathoracic pressure in order to produce a pressure–volume curve for each subject.

In all, 10 normal men, 6 normal women, and 16 patients of both sexes with heart disease, mainly rheumatic, were examined. It was found that the pressure required to produce a change in lung volume of 100 ml. was significantly greater in patients with heart disease. This factor was found to show a high degree of correlation with the reciprocal of the vital capacity both of normal subjects and of patients, but no relation was found between the reduction in vital capacity and the increased resistance to air flow.

Comparison of the pressure–flow relationships in patients with heart disease when breathing the two gas mixtures showed that tissue friction was a negligible factor and that the degree of movement of the lungs was determined by the degree of resistance to gas flow. Since there may be no increase in resistance to air flow in patients with heart disease and exertional dyspnoea the authors conclude that the latter is most closely related to a reduction in vital capacity and to the altered elastic properties of the lung; on the other hand it is thought likely that increased resistance to air flow may play an important role in the dyspnoea of cardiac asthma.

H. E. Holling

920. Ventricular Function. VI. Balance of Left and Right Ventricular Output: Relation between Left and Right Atrial Pressures
E. BERGLUND. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 381–386, Sept., 1954. 5 figs., 29 refs.

The object of this study, which is reported from Harvard School of Public Health, Boston, was to investigate the mechanism responsible for maintaining the balance of output between the left and right ventricles and to test the hypothesis that the relation between ventricular filling pressure and ventricular stroke work provides the basis for this mechanism. The relation between the left and right atrial pressures was studied in dogs and the effect on it investigated of increasing the outflow resistance of each ventricle independently, of restricting coronary flow on one side, and of changing the intrapericardial pressure. It was found that when one ventricle was subjected to stress its filling pressure increased in relation to that of the other ventricle. It is stated that "the varying relationship between the two atrial pressures, when integrated with Starling's law of the heart, explains how the two ventricles maintain output balance during varying conditions."

A. I. Suchett-Kaye

921. The Heart in Acute Glomerulonephritis
T. R. MURPHY and F. D. MURPHY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 510–532, Sept., 1954. 3 figs., 28 refs.

The cardiac changes in acute glomerulonephritis were studied at Milwaukee County Hospital, Wisconsin. In the authors' view cardiac involvement is indicated by the presence of one, or any combination, of the following: (1) clinical heart failure; (2) radiological evidence of

cardiac enlargement of the heart; and (3) electrocardiographic (ECG) abnormalities. On this basis cardiac changes were found in 41 out of 88 cases of glomerulonephritis. Heart failure, which was present in 22 of the cases, appeared to be more frequent in patients over 21 years of age and in those with moderate or severe hypertension, although hypertension itself was not considered to be the sole cause of failure. Cardiac failure occurred in 9 of 16 patients with convulsions. The most frequently observed abnormalities in the ECG were T-wave changes in Lead 1. The authors point out that heart failure may not always be recognized because the oedema of acute nephritis may obscure distension of the neck veins. Further, it may not be suspected since little is known about the incidence of heart failure in acute nephritis. *James W. Brown*

CONGENITAL HEART DISEASE

922. **Atrial Septal Defects. A New Surgical Approach and Diagnostical Aspects.** [In English]
V. O. BJÖRK, C. CRAFOORD, B. JONSSON, S. R. KJELLBERG, and U. RUDHE. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **107**, 499–515, July 6, 1954. 8 figs., 14 refs.

Before surgical treatment of an atrial septal defect can be undertaken, catheterization of the heart is always necessary in order to verify the diagnosis, to calculate the size of the shunt, and to measure the pulmonary arterial pressure. It is noted, however, that where the defect is close to the valvular plane the main stream of blood is directed towards the tricuspid orifice and is expelled directly into the right ventricle with negligible mixing in the right atrium, so that a ventricular septal defect may be wrongly suggested by the results of blood gas analysis. The authors, working at the Karolinska Institute and Hospital, Stockholm, have found the usual methods of angiocardiography unsatisfactory for the adequate radiological diagnosis of atrial septal defects and have therefore devised a new technique whereby the contrast medium is injected into the left atrium by means of a catheter passed through the defect via the saphenous vein. The catheter has multiple outlets directed backwards so that the contrast medium passes in the direction of blood flow through the defect and an unwanted reflux to the pulmonary veins is prevented. The whole amount of contrast medium (1·2 ml. per kg. body weight) must be injected in less than one second by means of an automatic pressure syringe, and exposures are made at a rate of at least 10 per second in each plane. Oblique projections are used to visualize the septal plane tangentially and perpendicularly. In addition, an inflatable balloon fixed to the catheter and filled with contrast medium is used to outline the defect and indicate its size. With this technique it is possible to demonstrate or exclude a complicating mitral stenosis, but a co-existing abnormal venous return cannot be excluded.

A new method is described for the closure of an atrial septal defect which is a modification of the operation devised by Sondergaard and Husfeldt. A right thoracotomy is performed through the bed of the 6th rib, the pericardium opened, and the venae cavae dissected free at their junction with the right atrium. A groove is then dissected between the atria from a point between the superior vena cava and the right superior pulmonary vein down to the inferior vena cava, continuing until the muscle bundles are seen crossing from one atrium to the other. This dissection is very important as it will prevent obstruction of the venae cavae or of the pulmonary veins when the suture is tied. Guided by a finger introduced through the right auricular appendage, a curved needle is then introduced at the root of the aorta 1 to 2 cm. behind the origin of the right coronary artery, passed subendocardially behind the defect until the valvular plane is reached, rotated forwards to avoid the coronary sinus, and brought out behind the inferior vena cava. If there is no septal rim in the valvular plane the needle is directed through the upper border of the interventricular septum. Rotation of the needle when the valvular plane is reached ensures that it will pass obliquely from the right side of the interventricular septum over to the left side, thus reducing the risk of damage to the bundle of His. The needle is brought out through the left atrial wall as close to the atrio-ventricular border as possible. The heavy (No. 4 or 5) silk thread which has been passed with the needle is then tied over a piece of fascia or muscle in the dissected groove between the cavae and the right pulmonary veins and drawn tight until the palpating finger finds the defect completely closed.

Of the 12 patients so treated, 10 have survived the operation and the immediate results seem satisfactory, although it is too soon yet to assess the end-results, the longest follow-up being 7 months. The article is fully illustrated, and detailed descriptions are given of 4 of the cases treated. *F. J. Sambrook Gowar*

923. **Ventricular Septal Defect, with a Note on Acyanotic Fallot's Tetralogy**
P. WOOD, O. MAGIDSON, and P. A. O. WILSON. *British Heart Journal* [*Brit. Heart J.*] **16**, 387–406, Oct., 1954. 15 figs., bibliography.

Although some workers have declared ventricular septal defect to be one of the commonest forms of congenital heart disease—a proportion as high as 37% has been reported—the authors of the present paper have found among patients investigated at the National Heart and Brompton Hospitals, London, since 1948 that ventricular septal defect (confirmed in most cases by cardiac catheterization) accounted for only 8% of 750 cases of congenital heart disease—a proportion nearly the same as that of coarctation of the aorta (7·5%). Moreover, few of these cases conformed to the classic type described by Roger (*maladie de Roger*) whose original description is here recalled.

The authors then review the main features in 60 fully confirmed cases comprising equal numbers of male and female patients, 46 of whom were under 15; 22 of the cases were judged mild, 18 moderate, 12 severe, and 8 were complicated by pulmonary hypertension; cases of Eisenmenger's complex were excluded. Clinically,

the patient's growth was usually normal and no associated abnormalities were found. The pulse was small in the severe cases, but a hyperdynamic left ventricular impulse was present in all but mild cases. A systolic thrill was almost invariable (90% of cases) and the authors state that a clinical diagnosis of ventricular septal defect (without pathological proof) should not be made in its absence. Similarly a loud systolic murmur along the left sternal border was recorded in all but 6 cases, and a functional diastolic mitral murmur in a like number. Radiologically, evidence of increased pulmonary blood flow and enlargement of the left heart was obtained. All severe cases showed electrocardiographic evidence of left and right ventricular enlargement, but when pulmonary resistance was raised, the right ventricle preponderated. Right bundle-branch block occurred in 12 cases (20%), but complete heart block in only one. Pulmonary blood flow increased with the severity of the lesion, as did also the difference in oxygen saturation between samples of pulmonary arterial and right atrial blood. In 8 cases with pulmonary hypertension the shunt was far less, pulmonary blood flow being only about double the systemic blood flow.

The differential diagnosis is discussed in detail. In mild cases and when a systolic thrill and murmur are almost the only signs, other possible conditions to be considered are: mild pulmonary stenosis, mild infundibular stenosis, acyanotic forms of Fallot's tetralogy, mild aortic and subaortic stenosis, mitral incompetence with anti-clockwise rotation, mild atrial septal defect, and so-called innocent left parasternal murmur (" whatever that may be "). Ten of the authors' cases of acyanotic Fallot's tetralogy are described in detail for comparison. Discussing the prognosis of ventricular septal defect the authors report that during a 5-year observation period there have been no deaths among the 60 cases described. One case of bacterial endocarditis only has occurred, the incidence being estimated at below 10%. The authors recommend that the term *maladie de Roger*, if retained at all, should be applied only to mild cases of ventricular septal defect.

[This is an important article which should be read in full by all interested in the subject.] *F. Starer*

924. **The Surgery of Infundibular Pulmonic Stenosis with Intact Ventricular Septum (a Type of " Pure " Pulmonic Stenosis)**

R. P. GLOVER, T. J. E. O'NEILL, H. GONTIGO, T. C. MCAULIFFE, and C. R. E. WELLS. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 481–503, Nov., 1954. 8 figs., 40 refs.

The authors present, from St. Christopher's Hospital for Children and the Presbyterian Hospital, Philadelphia, 6 cases of " pure " pulmonary stenosis in which the constriction was in the infundibulum rather than at the level of the valve. The differential diagnosis of pure pulmonary stenosis and of the trilogy of Fallot is discussed. The importance of exact location of the site of obstruction in the right ventricular outflow tract is emphasized. For this the authors use first a small malleable probe and then a small urethral sound, these instruments being gently passed through the myocardium into the pulmonary artery. When the site of obstruction has been accurately located by palpation a long-shafted resector is introduced through a small (1 cm.) incision and the muscle is punched out with the rongeur, several bites being taken to ensure complete removal of the stenosing crest. The authors state that ideally, although pressure recordings taken at the time of operation are useful, they are not essential, as so much can be ascertained by simple palpation.

The postoperative changes which may be expected in a successful case are described. In the authors' opinion the best method of appraisal of the results is careful follow-up of the patients. In 25 cases treated so far by this method there have been no deaths. In the 6 cases more fully described in this paper 4 of the patients are now asymptomatic and the other 2 are considerably improved. *J. R. Belcher*

925. **Pulmonic Valvular Stenosis. Results and Technique of Open Valvuloplasty**

H. SWAN, H. C. CLEVELAND, H. MUELLER, and S. G. BLOUNT. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 504–515, Nov., 1954. 1 fig., 16 refs.

Pulmonary stenosis, whether in combination with a patent interatrial septum or as an isolated lesion, is not a benign condition, and the present authors recommend surgical treatment in all cases in which the systolic blood pressure in the right ventricle exceeds 75 mm. Hg. They note that the results obtained with the " blind " approach are unpredictable, the pressure gradient across the stenosed area often remaining high despite an apparently adequate operation. They have also been dissatisfied with the results of operation by the transventricular route, and have therefore developed a method whereby the pulmonary valve can be divided under direct vision through the pulmonary artery. They describe this technique in detail; in essence it consists in opening the pulmonary artery under hypothermia after the aorta has been clamped and the venae cavae occluded with tapes. The valve can be clearly seen and two incisions are made at 180 degrees to each other from the valve opening right out to the ring, this forming a sort of bicuspid valve. A finger should always be passed through the valve into the ventricle to confirm the absence of infundibular stenosis.

Of 7 patients operated on at the University of Colorado School of Medicine, Denver, by this technique, all have survived, and the postoperative catheterization studies have shown that the results, as judged by determination of pressure gradients, are better than those in cases in which the blind technique was used. *J. R. Belcher*

926. **Simple Pulmonary Stenosis**

D. W. BARRITT. *British Heart Journal* [*Brit. Heart J.*] **16**, 381–386, Oct., 1954. 5 figs., 13 refs.

The author reviews the clinical features in 33 cases of simple pulmonary stenosis in children seen at the Royal Infirmary, Bristol, and followed up for periods of 5 to 21 years. Of the 33 patients (16 male and 17 female), 23 had no symptoms and led a completely normal life,

9 complained of dyspnoea, and one of dyspnoea and chest pain on exertion. The following were the main signs observed: cyanosis in 4 cases (these patients had haemoglobin levels above 115%), clubbing of the fingers in 3, conspicuous " a " waves in 7, and a right ventricular impulse in 11. In all the cases a pulmonary systolic murmur was present and in 11 the second sound was split. Radiologically, the heart was enlarged in only one case, but post-stenotic dilatation of the pulmonary artery was noted in 19. The electrocardiogram was either normal or showed right ventricular dominance, with or without T inversion. Right ventricular pressure in the 8 cases in which it was determined ranged from 40 to 180 mm. Hg.

During the period of observation 4 of the patients complained of increasing breathlessness, and 2 developed subacute bacterial endocarditis. The author concludes that many of these patients are likely to survive to later decades and remain symptomless; operation is not indicated in those who show no evidence of right heart stress.

[This paper should be compared with that by Dimond and Lin (*Ann. intern. Med.*, 1954, **40**, 1108 ; *Abstracts of World Medicine*, 1954, **16**, 470) in which 20 similar cases are described.] *F. Starer*

927. **Pulmonary Stenosis with Left to Right Shunt**
O. MAGIDSON, R. S. COSBY, S. P. DIMITROFF, D. C. LEVINSON, and G. C. GRIFFITH. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 311–321, Sept., 1954. 4 figs., 25 refs.

Details are presented from Los Angeles County Hospital (University of Southern California) of 14 cases in which stenosis of the pulmonary valve was associated with an additional defect causing a left-to-right intracardiac shunt, this being in 2 an anomalous pulmonary venous return into the right auricle, and in 8 an atrial and in 4 a ventricular septal defect. Symptoms were mild or absent in all 14 cases, and the physical signs were generally those typical of mild pulmonary stenosis. All had a systolic murmur to the left of the upper sternum, with an accompanying thrill in 11 cases, the pulmonary second sound being normal or diminished rather than accentuated. In all there was electrocardiographic evidence of right ventricular hypertrophy. An associated atrial septal defect was suggested by the presence of partial right bundle-branch block in 4 cases and abnormal pulsation of the pulmonary arteries in a fifth case. A ventricular septal defect was correctly diagnosed from the low site of the murmur in 2 cases. Cardiac catheterization showed varying degrees of severity of pulmonary valvular stenosis in all cases. In 3 the right ventricular systolic pressure was above 100 mm. Hg; the right ventricular diastolic pressure and right auricular pressure, however, were normal and the characteristic giant " a " waves were therefore not present in pressure tracings from the systemic veins.

The authors discuss their findings and express the opinion that in the 8 cases in which there was interatrial communication this probably occurred through a true atrial septal defect rather than through a patent foramen ovale, for the latter probably only transmits shunts from right to left, and only when this is forced by an increase of pressure in the right auricle. Patients with an interatrial or interventricular communication are liable to develop cyanosis if right ventricular pressure is sufficiently raised. They do not recommend surgical intervention unless pulmonary stenosis is severe, for when this is moderate its presence may protect the lungs against the deleterious effects of greatly increased pulmonary blood flow. In 3 of their cases in which right ventricular pressure was high, pulmonary valvotomy was successfully performed. *J. A. Cosh*

928. **Absence of the Left Pulmonary Artery. A Report of Six Cases with Autopsy Findings in Three**
J. S. MCKIM and F. W. WIGLESWORTH. *American Heart Journal* [*Amer. Heart J.*] **47**, 845–859, June, 1954. 8 figs., 18 refs.

The authors report, from the Children's Memorial Hospital (McGill University), Montreal, 3 cases of absence of the left pulmonary artery confirmed at necropsy and 3 presumptive cases in patients still living (all aged 5 years), and on the basis of these and 11 cases reported in the literature in which the absence of one or other pulmonary artery was found they discuss the anatomical, clinical, angiocardiographic, and radiographic features of this condition.

In practically all the reported cases the anomaly has been associated with some other form of congenital heart disease, particularly Fallot's tetralogy. As a rule the pulmonary artery has been absent on the side opposite to that of the aortic arch, so that when the left pulmonary artery is absent the aortic arch is usually right-sided. In all 3 of the authors' cases coming to necropsy there was a right aortic arch and a left innominate artery, with an obliterated vessel (almost certainly a left ductus arteriosus) running from the latter to the hilus of the left lung; the intrapulmonary distribution of the branches of this vessel was identical with that of a normal left pulmonary artery.

Cases may be recognized radiologically by noting a smaller lung on one side combined with increased translucency due to diminished vascular shadows on the pathological side. It has been shown that although the ischaemic lung is responsible for about one-third of the total ventilation, its uptake of oxygen is only about 6% of the total oxygen consumed. The authors also point out that a patent ductus arteriosus may join the innominate artery to the homolateral pulmonary artery, and may therefore be right-sided when the aortic arch is left-sided; cases of bilateral patent ductus have also been recorded.

An incidental, but highly important, observation was the finding of strictly normal peripheral pulmonary arteries and arterioles on the affected side in the authors' third case (a case of Eisenmenger's complex) although these vessels on the unaffected side were typically hypertrophied; this offers unique evidence that the hypertension of Eisenmenger's complex does not depend on congenital structural alterations in the peripheral pulmonary vascular bed. *Paul Wood*

929. **Pulmonary Arterial Pressure in Acyanotic Congenital Heart Disease**
R. J. SHEPHARD. *British Heart Journal* [*Brit. Heart J.*] 16, 361–374, Oct., 1954. 8 figs., 26 refs.

The author reports a study carried out at Guy's Hospital, London, by cardiac catheterization of the relationship of blood pressure to blood flow in the pulmonary circulation in 24 cases of patent ductus arteriosus, and compares the results with those in 17 cases of atrial septal defect and 14 of ventricular septal defect.

Of the 22 cases of patent ductus arteriosus in which the catheter could be introduced into the pulmonary artery, 10 showed systolic pressures within normal limits (11 to 29 mm. Hg), 6 a slight rise (31 to 45 mm. Hg), and 6 a moderate rise (45 to 80 mm. Hg); in 10 out of 17 of these in which the diastolic pressure was also measured it was greater than normal. Of the 17 cases of auricular septal defect, the pulmonary artery was entered in 12; only 5 of these had a normal systolic pressure, while in one the rise was slight, in 3 moderate, and in 3 severe (over 80 mm. Hg). The diastolic pressure in this group showed some increase in those with a raised systolic pressure, but there was a tendency to a wider range of pulse pressure than in the cases of patent ductus arteriosus. In the 14 cases of ventricular septal defect the pulmonary arterial pressure was normal in 2, slightly raised in 2, moderately raised in 3, and markedly raised in 7. The high incidence of pulmonary hypertension in this condition is explained by the fact that, except in small defects, the right ventricular pressure approximates to that in the left ventricle. It was not possible to correlate the size of the shunt at the time of the examination with the pulmonary arterial pressure.

In all 3 types of case there was an unexplained difference of a few mm. Hg between the right ventricular systolic pressure and that in the pulmonary artery. The higher pressures in the cases of atrial septal defect may be explained in part by the higher average age of the patients in this group (19·6 years, compared with 12·3 years for those with patent ductus arteriosus and 15·6 years for those with atrial septal defect) and in part by the fact that the increased flow is concentrated in the systolic phase of the cycle. The pulmonary arteriolar resistance may be low, normal, or high in all three types; with increasing age this resistance tends to increase, presumably in correspondence with the progressive development of structural changes in the small vessels of the lung.

C. Bruce Perry

930. **The Syndrome of Patent Ductus Arteriosus with Reversal of Flow**
D. S. LUKAS, J. ARAUJO, and I. STEINBERG. *American Journal of Medicine* [*Amer. J. Med.*] 17, 298–310, Sept., 1954. 5 figs., 31 refs.

From the New York Hospital (Cornell Medical Center), New York, the authors describe 4 cases in which patency of the ductus arteriosus was combined with pulmonary hypertension sufficiently great to drive venous blood from the pulmonary artery into the aorta. The shunt was thus from right to left, a reversal of the usual state of affairs in uncomplicated patent ductus. All 4 patients, who were aged 22, 24, 26, and 37 respectively, had suffered for some years from some degree of dyspnoea and showed at some stage the pathognomonic sign of cyanosis of unequal distribution: typically, the toes were cyanosed and clubbed and the fingers were not, or only slightly. In one case the left hand showed more cyanosis than the right. In none was the continuous murmur of uncomplicated patent ductus present, although this had been heard in childhood in one case.

On the basis of these 4 cases and of 12 others selected from the literature the authors conclude that physiological and clinical features in these cases are sufficiently characteristic to warrant the designation of a syndrome. The diagnosis can be confirmed unequivocally by cardiac catheterization and angiocardiography. In the authors' cases cardiac catheterization confirmed severe pulmonary hypertension in all; all had a right-to-left shunt, causing femoral arterial blood to have a lower oxygen saturation than right brachial arterial blood. In 3 of the 4 cases blood was evidently passing in both directions through the ductus, the presence of this left-to-right shunt causing a higher oxygen saturation in the pulmonary artery than in the right ventricle. Angiocardiography showed simultaneous opacification of the pulmonary artery, the patent ductus, and the descending aorta.

Surgical treatment of such cases has been limited and is always hazardous. In 3 of the 4 present cases ligation of the ductus was attempted: in 2 the operation had to be abandoned (in one case because of extreme friability of the ductus) and the third patient died after ligation. The pathogenesis of the pulmonary vascular lesions is discussed. The authors believe that pulmonary hypertension in these patients arises originally as a result of the large left-to-right shunt and the sustained heavy flow of blood to the lung. Later, when organic changes have developed in the pulmonary arteries, the amount of this flow falls somewhat. In younger patients with this syndrome, however, they suggest that pulmonary hypertension may have a congenital origin. In spite of the risks of surgery they believe that a cautious attempt at ligation is justified in those patients in whom a left-to-right shunt still persists.

J. A. Cosh

DISTURBANCES OF RHYTHM AND CONDUCTION

931. **Depression of the Heart by Quinidine and its Treatment**
T. R. L. FINNEGAN and J. R. TROUNCE. *British Heart Journal* [*Brit. Heart J.*] 16, 341–350, Oct., 1954. 7 figs., 42 refs.

Amongst 115 patients treated with quinidine for cardiac arrhythmia at Guy's Hospital, London, 3 developed severe reactions, which were fatal in one. The main changes noted electrocardiographically in these cases indicated depression of the bundle and nodal tissue. In 5 further cases electrocardiographic abnormalities were noted in the absence of symptoms of collapse. These abnormalities again indicated depression of various parts of the nodal or conducting tissue, but in some cases

ventricular extrasystoles or tachycardia were present in addition. It was found that the experimental administration of quinidine to rabbits produced effects similar to those seen in man. Various substances—adrenaline, noradrenaline, phenylephrine, caffeine, ephedrine, and acetylcholine—were used in an attempt to revive the heart depressed by quinidine, adrenaline being the most effective both in the isolated perfused heart and in the intact animal. The application of these findings to the treatment of cardiac arrest in man following the administration of quinidine is discussed. *C. Bruce Perry*

932. **Studies on Cardiac Arrest: the Relationship of Hypercapnia to Ventricular Fibrillation**
W. C. SEALY, W. G. YOUNG, and J. S. HARRIS. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 447–462, Nov., 1954. 9 figs. 22 refs.

It has been suggested that one of the causes of sudden cardiac arrest during surgical operation may be hypercapnia. In this paper the authors summarize the results of a series of experiments carried out at Duke University, Durham, North Carolina, designed to elucidate this problem.

In the first experiment 12 dogs were allowed to breathe a mixture of carbon dioxide (20%) and oxygen (80%) and the vagus was stimulated until vagal "escape" occurred; the duration of asystole was used as a measure of cardiac response. Hypercapnia markedly increased the duration of asystole in all cases, and in 9 dogs, when the proportion of CO_2 was increased to 30 to 40%, the duration of asystole varied directly with the degree of hypercapnia. (Acute hypoxia actually decreased the duration of asystole.) In none of these animals did cardiac arrest occur during hypercapnia, but in 3 cases ventricular fibrillation developed in the immediate post-hypercapnic period on return to breathing room air. As the electrocardiographic (ECG) changes—namely, alteration in T wave, increase in conduction time, ventricular extrasystoles, and A-V dissociation—were those associated with hyperkalaemia, the plasma potassium content was further investigated in 21 dogs which were anaesthetized with pentobarbitone, given 30 or 40% CO_2 in oxygen for 3 to 5 hours, and then suddenly removed to room air. It was found that the plasma potassium level increased during CO_2 administration and rose still further during the immediate post-hypercapnic period; in 14 animals the ECG changes were significant, but ventricular fibrillation did not occur until transfer to room air. Among other experimental results reviewed are those occurring in dogs after prolonged periods of hypoxia and of continuous infusion of potassium, as well as the effect on these changes of the administration of adrenaline, an adrenolytic agent, and hypertonic glucose and saline infusions. Finally, the records of 36 patients in whom cardiac arrest occurred during operative procedures were reviewed. Of 24 of these cases in which no clear cause for the cardiac arrest was apparent, 10 occurred as the wound was being closed, 11 in the middle of a thoracic operation, one just after release of a limb tourniquet which had been in place for 45 minutes, and 2 occurred during induction of anaesthesia. It is thought that hypercapnia might have occurred in the first 22 of these cases.

In summing up these findings the authors suggest that the release of adrenaline, the production of hyperkalaemia by infusion of stored blood or by the sudden release of potassium from ischaemic muscle on removal of a tourniquet, hypercapnia due to inadequate ventilation (for example, in cyclopropane anaesthesia), and lastly, the too rapid return to room air after breathing anaesthetic mixtures may all play a part in causing otherwise unexplained cardiac arrest. It is stressed that a careful watch on the ECG recording gives warning of impending post-hypercapnic ventricular fibrillation, and that this can be prevented by the prompt intravenous infusion of 20% glucose and 3% sodium chloride solution.

(In the interesting discussion which followed this paper a case was described in which a child survived after the occurrence of ventricular fibrillation lasting for 1 hour 50 minutes.) *D. D. C. Howat*

ENDOCARDIUM

933. **A Case of Infective Endocarditis Confined to the Tricuspid Valve Resulting from Septic Endarteritis of an Arterio-venous Aneurysm.** (К вопросу об изолированном поражении трехстворчатого клапана при затяжном септическом эндокардите, развившемся в результате септического эндартериита артериовенозной аневризмы)
E. K. BEREZOVSKAYA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **32**, 80–86, Oct., 1954. 8 figs., 4 refs.

A case is described in which septic endocarditis involving the tricuspid valve developed as a result of septic endarteritis of an arterio-venous aneurysm of the left subclavian vessels. The aneurysm resulted from a wound caused by a bomb-splinter in 1944 when the patient was 14. In 1950 he complained of breathlessness and pain in the cardiac region. The arterial blood pressure was 120/55 mm. Hg, and operation for closure of the aneurysm was advised, but refused. In December, 1951, his condition had deteriorated and his temperature rose at times to 40° C. (104° F.). In July, 1952, he requested operation. He then had cyanosis of the neck, lips, and ears, and acrocyanosis. His pulse rate was 120 per minute, the heart was dilated, with systolic and diastolic murmurs at the apex and over the aortic area, the liver was enlarged and tender, and the spleen also enlarged. He was given penicillin, cortisone, and intravenous glucose, and the aneurysm was ligated, but the vessels could not be dissected and separated owing to adhesions to the surrounding tissues and the nervous plexus. There was severe haemorrhage during the operation, which was arrested by application of a muscle graft. His condition became worse, and he died 4 hours after the operation.

Post mortem 250 ml. of liquid blood was found in the left pleural cavity and 1 litre of straw-coloured fluid in the peritoneum. The spleen was enlarged and contained 2 large infarcts, the kidneys were ecchymotic, and there was a nutmeg liver. Vegetations were present on the tricuspid valve, with dilatation of the atrio-ventricular

orifice, streptococci being isolated from the vegetations. Evidence of septic endarteritis was found in the left subclavian artery in the region of the aneurysm, and the wall of the vein was thinned and poor in elastic fibres. Thrombotic deposits were found on the wall of the arterio-venous fistula, which in one part showed inflammatory infiltration of all three coats.

L. Firman-Edwards

934. **Treatment of Subacute Bacterial Endocarditis**
P. A. BUNN and E. T. COOK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 487–500, Sept., 1954. 13 refs.

Antibiotics have been used with success in the treatment of subacute bacterial endocarditis for about 9 years, the recovery rate of patients suffering from this disease being now approximately 70%. The treatment and subsequent course of the disease in 48 consecutive cases are described in this paper from the Medical School of the State University of New York, Syracuse. In 10 cases no causative organism was isolated. Penicillin was given in all except one of the 48 cases and in 16 streptomycin was given as well. In general the dose of the antibiotic was determined by measuring the sensitivity of the causative organism. This specific antimicrobial therapy was continued for 3 weeks after all signs of infection had disappeared.

There were 15 deaths, 14 of which were directly attributable to the infection; failure in these cases was due to inadequate therapy, the development of resistant organisms, irreversible cardiac failure, or gross anatomical changes. It is pointed out that treatment cannot be expected to do more than eradicate the causative organism, and therefore early diagnosis and prompt administration of the appropriate antibiotic are essential if irreversible anatomical changes are to be prevented. The long-term prognosis is poor in patients in heart failure or those with aortic incompetence, and reinfection is always possible. The authors do not consider that the results of treatment of subacute bacterial endocarditis have improved appreciably in the past 5 years.

James W. Brown

CHRONIC VALVULAR DISEASE

935. **The Clinical Features of Aortic Stenosis**
A. M. MITCHELL, C. H. SACKETT, W. J. HUNZICKER, and S. A. LEVINE. *American Heart Journal* [*Amer. Heart J.*] **48**, 684–720, Nov., 1954. 24 refs.

This rather lengthy survey of the clinical features of aortic stenosis was prompted by the possibility of surgical treatment becoming available in the near future. The 533 cases studied were collected from the records of the Peter Bent Brigham Hospital (Harvard Medical School), Boston, for the period 1913–52, and comprise 131 cases of pure aortic stenosis, 224 of aortic stenosis with incompetence, 149 of aortic and mitral stenosis with or without aortic incompetence, and 29 of aortic, mitral, and tricuspid stenosis.

The authors believe that 90% or more of cases of aortic stenosis, even with calcification, are rheumatic in origin. Pure aortic stenosis was more common in the male, and the average age at death was 65·3 years, whereas association with aortic incompetence reduced the average age at death to 52·5 years. Angina was present in 159 cases in all (29·8% of the whole series), and in 36·7% of cases of pure aortic stenosis; after the onset of angina the average duration of life was about 4 years. Subacute bacterial endocarditis occurred in 10% of cases in the whole series.

[While nothing new emerges from this study, it merits attention as an assessment of present knowledge of the clinical features and course of aortic stenosis.]

James W. Brown

936. **Experiences in the Surgical Treatment of Aortic Stenosis**
W. H. MULLER, A. A. KATTUS, J. F. DAMMANN, and R. T. SMITH. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 516–535, Nov., 1954. 9 figs., 9 refs.

The authors give a brief history of the surgical treatment of aortic stenosis, and present the results in 25 of their cases subjected to aortic valvotomy by the transventricular route at the University of California Medical Center and various hospitals in Los Angeles. The patients were divided into five classes according to the severity of their symptoms; in the authors' opinion all patients except those with the mildest disability should be considered for treatment by aortic valvotomy, due consideration naturally being given to the state of the mitral valve and to the degree of aortic incompetence. They stress the desirability of early operation, since delay increases the risk of sudden ventricular failure. [Their operative technique, which is described in detail, differs little from that of Bailey, except that the authors use a very much simpler type of valve dilator.]

Of their 25 patients, one group of 16 had "pure" aortic disease; calcification of the valve was present in 13 of these cases and also in 8 out of the 9 in the second group, in which associated mitral disease was present. The patients' ages ranged from 14 to 63 years. There were 4 operative deaths, 2 in each group. The authors stress the difficulty of objective postoperative assessment, but from the patients' statements conclude that the results in the cases of isolated aortic disease were better than in those with associated mitral valve lesion. Although in no case did the aortic murmur entirely disappear, more than half the patients surviving the operation were deemed to have "excellent improvement". The authors conclude that the early results are encouraging.

J. R. Belcher

937. **Indications and Contraindications for the Surgical Treatment of Mitral Stenosis.** (Клинические показания и противопоказания к хирургическому лечению митрального стеноза)
I. N. RYBKIN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **32**, 32–38, Oct., 1954. 22 refs.

In a series of 300 necropsies on patients dying of heart disease, the mitral valve was involved in 85%, yet pure stenosis was present in only 5% and pure mitral insufficiency in only 2%. Estimates in the literature of the incidence of pure stenosis range from 1·3 to 12·5%. The surgical relief of this condition began to be considered at

the beginning of the present century, and Lauder Brunton in 1902 first suggested division of the adherent cusps by means of an instrument introduced through the great vessels. In 1912 Tuffe dilated a stenosed aorta with his finger by invagination of its wall, and in 1925 Souttar dilated a stenotic mitral orifice by means of a finger inserted through an incision in the left auricular appendix, the patient living 5 years. Yarotsky in 1925 recommended the relief of mitral stenosis by creating an artificial opening through the fossa ovalis, basing his suggestion on the favourable progress of mitral stenosis in patients with a patent foramen ovale.

Available measures of surgical relief may be divided into direct and indirect methods, the latter including thyroidectomy and the formation of extra- and intracardiac shunts (such as the production of tricuspid insufficiency or of an interatrial orifice) or anastomosis between the pulmonary and azygos veins. Direct surgical relief by valvotomy or commissurotomy has become possible in recent years, and the author reviews in some detail the results obtained, in Russia and elsewhere, since 1951. Careful selection of cases is necessary in order to obtain good results and to avoid serious complications, and for this purpose the author regards the following as essential: (1) accurate diagnosis and assessment of the degree of stenosis; (2) determination of the presence or absence of mitral incompetence, and its degree, if present; and (3) determination of the presence or absence of vascular changes in the pulmonary vessels. Caution should be observed in recommending or undertaking operation in the presence of calcification of the valves or of thrombi in the auricular appendix, in cases of hypertension, and in cases with tricuspid incompetence. Operation is contraindicated in cases with active rheumatism, bacterial endocarditis, well-marked mitral or aortic incompetence or advanced decompensation with enlargement of all the cavities of the heart.

L. Firman-Edwards

938. **The Natural History of Mitral Stenosis**
J. K. Wilson and W. F. Greenwood. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **71**, 323–331, Oct., 1954. 1 fig., 22 refs.

In order to determine the prognosis in mitral stenosis when not treated surgically, the records of all patients admitted to the Toronto General Hospital with that diagnosis between 1937 and 1941 were reviewed in 1953 and the patients traced if possible. Out of 194 such patients, contact had been lost with 23, and of the remaining 171, 51 were alive. In 153 of the 171 cases the mitral valve alone had been affected. Of 107 patients originally admitted because of cardiac symptoms, 100 had died before 1953.

The course of the disease may be divided into five stages: (I) active rheumatic disease; (II) latent or asymptomatic heart disease (15 out of 19 patients seen at this stage on admission for other causes remained asymptomatic after 15 years); (III) slight cardiac disability (of 20 patients so classified, 5 had died, and in 3 the disease had progressed to later stages); (IV) severe pulmonary congestion, as revealed by acute pulmonary oedema, orthopnoea, and nocturnal dyspnoea, or "one-flight, one-block" dyspnoea (there were 117 cases in which it was possible to determine the date of onset of this stage, which was sometimes precipitated by some factor such as pregnancy or the onset of auricular fibrillation); (V) right heart failure (the date of onset of which could be determined in 100 cases). After the onset of Stage IV, 16% of patients died within 6 months and 50% within 5 years. After the onset of Stage V, 24% of patients died within 6 months and 50% within 3 years. Of 99 patients with severe pulmonary congestion who would now have seemed suitable subjects for valvotomy, 16 died within 6 months, 45 within 5 years, and 77 within 15 years.

The average age at death of 120 patients was 45·8 years, 38% dying after the age of 50 and 13% after the age of 60. Whereas death in young persons is frequently associated with active rheumatic carditis, over the age of 30 years it is due to mechanical factors. It is recommended that valvotomy should be performed as soon as possible after the appearance of severe pulmonary congestion, because 16% of patients die within 6 months of this development, whereas the operative mortality is only about 6%. The risk of operation is greater in cases of congestive heart failure, but may be justified by the ultimate results.

R. S. Stevens

939. **Mitral Valvular Disease Associated with an Interatrial Communication.** (Les valvulites mitrales associées à la communication interauriculaire)
Y. Bouvrain and A. Sibille. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 3414–3424, Oct. 6, 1954. Bibliography.

Reviewing 91 cases of mitral valvular disease associated with an interatrial communication collected from the literature, together with 5 of their own previously reported with Soulié (*Arch. Mal. Cœur*, 1954, **47**, 97), the authors stress the need for accurate diagnosis of the condition in view of the recently acquired possibility of surgical treatment. The embryology is recalled; it is shown that a persistent ostium secundum (ovale) is three times as common as a persistent ostium primum, and that the mitral valve is affected by endocarditis twice as frequently as by a congenital abnormality. The clinical features were found to vary widely; signs of the septal defect may be clear or absent, while those of mitral disease are often diminished by the presence of the first lesion. Fluoroscopy is of paramount importance, and shows almost invariable enlargement of the heart, especially of the right side, pulsatile expansion of the median arc with dilatation of the pulmonary arteries, a small aorta, and backward compression of the oesophagus, the heart being sometimes pyriform and median as in pericarditis; yet the influence of mitral stenosis on this picture is negligible.

Cardiographic findings were available in one-third of the cases described. All except three revealed right-sided preponderance, but the incidence of right bundle branch block could not be determined. Cardiac catheterization, in the few cases in which it was employed, gave conclusive evidence of the presence of septal defect,

whereas angiocardiography was of little help. The authors point out that if auscultation yields unequivocal evidence of mitral stenosis the septal defect can readily be diagnosed; serious difficulty arises, however, when the septal defect is undoubted but the signs of mitral disease are inconclusive. In the 96 cases reviewed death, at an average age of 40 years, was usually due to congestive heart failure, but infants may die from pulmonary oedema. One of the patients described survived to the age of 82.

R. S. Stevens

940. **The Mechanism of the Signs and Symptoms of Mitral Valve Disease**

R. GORLIN. *British Heart Journal* [*Brit. Heart J.*] **16**, 375–380, Oct., 1954. 3 figs., 7 refs.

The author, writing from St. Thomas's Hospital, London, summarizes the known facts regarding the haemodynamics of mitral valve disease. The normal mitral valve is a fixed orifice with an area of about 5 sq. cm., but this may be reduced to 0·5 sq. cm. in disease; an area of 1·5 sq. cm. appears to be the critical value. The relation of blood flow through the valve to pulmonary "capillary" pressure is shown in a graph. As the area decreases, "capillary" (that is, atrial) pressure rises in order to maintain adequate flow rates. When pressure exceeds 30 mm. Hg pulmonary oedema develops. Tachycardia, by allowing only short intervals of flow during diastole, is frequently responsible for the onset of pulmonary oedema. Pulmonary capillary hypertension leads after a time to organic changes in pulmonary end-arteries. This at first is compensated for by hypertrophy of the right ventricle, but eventually this also fails; pulmonary resistance in some cases may be ten times the normal.

The intensity of the mitral diastolic murmur is no indication of the severity of the stenosis. When the valve is incompetent the left ventricle compensates for the leak if the state of the myocardium allows this. Where stenosis and incompetence coexist the former is often relatively mild. Nevertheless, systemic blood flow is necessarily reduced, resulting in symptoms of fatigue and moderate dyspnoea.

[This excellent summary of the subject is somewhat marred by the teleological viewpoint adopted by the author, since this outlook helps to gloss over some of the difficulties as yet unexplained.] *F. Starer*

941. **Myocardial Ischemia during Mitral Commissurotomy**

J. G. MUDD, J. J. INKLEY, and C. R. HANLON. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 330–336, Sept., 1954. 6 figs., 26 refs.

The occurrence of cardiac arrhythmia during thoracic surgery or cardiac catheterization is not uncommon. In this paper from St. Louis University, Missouri, the authors report the appearance of electrocardiographic abnormalities in 6 out of 30 patients undergoing mitral valvotomy which were related in time to the placing of a clamp on the appendix of the left auricle and were, the authors believe, probably caused by pressure on the left coronary artery. The abnormalities consisted of ST elevation and the appearance of a Q wave, and in 2 instances were quickly followed by ventricular tachycardia and fibrillation. When the surgeon was warned and moved the clamp, reversion towards normal occurred; in one case, however, electrical defibrillation and cardiac compression had to be carried out. No permanent changes were noted in the electrocardiograms. As only one lead was recorded in each case and artefacts were common, interpretation was difficult, but temporary ischaemia of the anterior wall of the left ventricle was thought to have occurred. The electrocardiograms reproduced show changes very similar to those seen in anterior myocardial infarction.

The authors stress the importance of electrocardiographic observation during operations on the mitral valve, particularly at the time of clamping of the auricular appendix, as the recording may give warning of impending ventricular fibrillation which may thus be avoided. *J. A. Cosh*

LYMPHATIC CIRCULATION

942. **Lymphangiography in Clinical Surgery and Particularly in the Treatment of Lymphoedema**

J. B. KINMONTH. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **15**, 300–315, Nov., 1954. 9 figs., 12 refs.

The author describes two techniques for the visualization of the lymphatic vessels which he has used in the study of lymphatic function, the first being visual lymphangiography, using coloured dyes, and the second *x*-ray lymphangiography.

For visual lymphangiography of the lower limb up to 2·5 ml. of an 11% (isotonic) solution of the dye "patent blue violet" is injected into the sole of the foot, both under the skin and deeply into the muscles, the needle being moved about during the injection. The site of injection is then massaged vigorously for half a minute or so and the ankle-, knee-, and hip-joints flexed fully and repeatedly for 3 or 4 minutes to compress the lymph trunks and drive their contents up the lymph pathways. Subsequent dissection shows the lymph trunks and nodes to be coloured blue-green by the dye. In 8 out of 10 patients with ulceration of the leg following deep venous thrombosis this method showed the lymphatics to be normal. Visual lymphangiography was also used to study the effect of radical mastectomy on the lymph trunks of the arm. It was found that the normal course of these lymphatics is such that it is impossible to preserve them and at the same time to carry out a satisfactory clearance of the axilla. On investigation of the lymph drainage of the ileum in Crohn's disease no evidence was found that obstruction in the lymph nodes was a primary cause of the disease. Similarly no element of lymphatic obstruction could be found in 3 cases of idiopathic hydrocele. *X*-ray lymphangiography has been unsuccessful hitherto because contrast medium injected into the tissues fails to enter the lymphatics in sufficient quantity. A satisfactory technique has now been developed in which a 70% solution of "pyelosil" (diodone) is injected

directly into a lymph vessel exposed at operation which has been coloured by a previous subcutaneous injection of patent blue violet. Radiographs of a normal leg after injection of diodone into the lymphatics are reproduced and show that the diameter of the lymph trunks remains uniform as they pass upwards (unlike that of the veins, which increases) and that they bifurcate as they pass proximally.

Studies of patients with idiopathic lymphoedema showed that the transmission of patent blue violet was defective in 12 out of 14 cases, while out of a total of 16 patients studied both by this method and by *x*-ray lymphangiography, 8 were found to have abnormally enlarged and tortuous lymphatics in which no valves could be shown. There was no evidence of localized obstruction in these vessels and " it is tempting to regard them as the lymphatic counterpart of varicose veins ". In the remaining 8 cases the lymphatics were not enlarged and in several of them lymph trunks could not be found despite a careful search. Other methods which have been used in the study of the lymphatic circulation in lymphoedema include the determination of the rate of absorption of serum protein labelled with radioactive iodine from the subcutaneous tissues and analysis of the oedema fluid; the results of these investigations are briefly mentioned, as also is the surgical treatment of the condition. The rare complication of chylous reflux is discussed.

A. G. Riddell

BLOOD VESSELS

943. **The Treatment of Obliterative Vascular Disease**
D. M. MORRISSEY. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **15**, 250–272, Oct., 1954. 8 figs., 48 refs.

The author discusses the treatment of occlusive vascular disease, with special reference to a series of 368 patients admitted to the United Birmingham Hospitals over the period 1946–53. Of these, 326 suffered from atherosclerosis or arteriosclerosis (17 of them being also diabetic) and 42 (all men) from Buerger's disease. The maximum incidence in the former group occurred among male patients aged 50 to 69 and among female patients aged 60 to 79; in the 42 cases of Buerger's disease the age of maximum incidence was between 30 and 39. In the latter group 27 patients presented with gangrene; it appears that in this disease extensive thrombosis occurs too rapidly for an effective collateral circulation to develop. In the whole series there were 87 cases of gangrene of the toes, but 15 of these retained normal pulsation in the foot, these cases being the most suitable for digital or transmetatarsal amputation. Intermittent claudication was the presenting symptom in 190 cases, in 44 of which no clinical evidence of trophic change was seen. The pathological changes in relation to the clinical state are discussed and illustrated.

In considering the various methods of treatment available the author states that a positive reaction in the affected limb in response to skin temperature tests is an indication that sympathectomy will probably effect lasting improvement, but its late effect on total blood flow is slight and on intermittent claudication doubtful, although it often relieves rest pain and allows healing of trophic ulceration. The treatment of an acute ischaemic episode should be energetic and include exposure of the limb to an environmental temperature of 20° C. to reduce metabolism, the administration of heparin and vasodilator drugs, and heating of the trunk and hands to encourage reflex vasodilatation. In choosing cases suitable for vascular grafting, careful selection is necessary. The best results are obtained in cases of isolated obstruction such as, for example, primary popliteal thrombosis, but these cases form only a small percentage of patients presenting with intermittent claudication. Vascular grafting is occasionally justifiable in acute ischaemia, particularly when deterioration continues in spite of conservative measures, the need for a major amputation becoming imminent, and there is arteriographic evidence of a segmental occlusion. The technique of preparing and storing grafts is described. The long-term results of grafting are finally governed, however, by the rate of progress of the underlying disease.

M. A. Birnstingl

HYPERTENSION

944. **Liver Function and Hypertension. Blood Pressure and Heart Weight in Chronic Hepatitis**
F. RAASCHOU. *Circulation* [*Circulation (N.Y.)*] **10**, 511–516, Oct., 1954. 2 figs., 28 refs.

On the basis of a post-mortem study carried out at the Kommunehospital, Copenhagen, the author claims that severely impaired hepatic function prevents the development of hypertension or may cause a pre-existing hypertension to subside. In diagnosing hypertension the author required the presence of cerebral haemorrhage or hypertrophy of the heart at necropsy as well as persistently abnormal blood pressure measurements during life. The series consisted of 102 women dying with chronic hepatitis and 93 women of comparable age dying from other diseases. The incidence of hypertension as determined by the above criteria was greater in the control series than in subjects with impaired hepatic function, and agreed with the expected incidence of hypertension in the general population.

J. Warwick Buckler

945. **Clinical Evaluation of Hydrallazine (Apresoline) alone and in Combination with Veriloid in the Treatment of Hypertension**
M. J. KERT, S. ROSENFELD, R. H. MAILMAN, J. P. WESTERGART, H. G. CARLETON, and E. HISCOCK. *Angiology* [*Angiology*] **5**, 318–328, Aug., 1954. 3 refs.

Sixty-four ambulatory patients were given oral hydrallazine (" apresoline ") for periods ranging up to 22 months. Side effects occurred in 42 patients, but the drug had to be discontinued in only 14. Eleven of those who had to discontinue the drug demonstrated their inability to tolerate it during the first few weeks (or doses). Only 3 had to discontinue the drug after taking it for 3 months. Procedures found to be helpful in alleviating

side effects consisted of: (*a*) restarting the drug at a lower dosage; (*b*) lowering an established high dosage by 25 to 50%; (*c*) combining " veriloid " with hydrallazine.

Of 43 patients who took hydrallazine alone for 3 to 22 months, 14, or 30%, had a good hypotensive response. An additional 12, or 28%, had only a fair hypotensive response. Fifteen of the 43 patients were given veriloid in addition to hydrallazine. This combination of drugs resulted in a good hypotensive response in 3 more patients. Thus 17, or 40%, of the original 43 patients obtained a good blood pressure result.

It would seem that the addition of veriloid to hydrallazine not only alleviated some of the side effects of the latter, but improved the hypotensive response to a degree that neither drug alone could achieve.—[From the authors' summary.]

946. **Hypertension and Its Control by Hexamethonium**
K. SHIRLEY SMITH, P. B. S. FOWLER, and V. EDMUNDS. *British Medical Journal* [*Brit. med. J.*] **2**, 1243–1250, Nov. 27, 1954. 28 refs.

The authors report on 83 patients with hypertension who were treated with hexamethonium bromide at Charing Cross Hospital, London, and followed up for periods of 6 months to 3 years. The drug was given parenterally to 51 patients and by mouth to 32; in 16 cases of the former group and 7 of the latter either treatment was abandoned or the patient died. Of the remaining 35 patients who received parenteral treatment, a " good " response in terms of reduced blood pressure was noted in 11 and a " fair " response in 12; of the 25 patients on oral treatment the response was " good " in 3 and " fair " in 5. However, many patients experienced relief of such symptoms as headache and angina despite an inadequate reduction in blood pressure. Side-effects consequent upon fall in blood pressure were: postural hypotension, muscular weakness, and the development of angina pectoris, intermittent claudication, or Raynaud's phenomenon. Effects due to the ganglion-blocking action of the drug were: dryness of the mouth, constipation (in one case straining at stool caused strangulation of a hernia), bladder disturbances, impotence, and paralysis of accommodation. In one patient hemiplegia and in another myocardial infarction developed shortly after injections of hexamethonium. A further patient complained of failing memory during hexamethonium therapy, and also noted slurring of speech about 2 hours after each injection.

K. G. Lowe

947. **The Medical Treatment of Hypertension**
J. G. BRAHAM and R. D. H. MAXWELL., *British Medical Journal* [*Brit. med. J.*] **2**, 1250–1254, Nov. 27, 1954. 2 figs., 48 refs.

Out of a total of 4,872 out-patients who attended the Royal Alexandra Infirmary, Paisley, for the first time during the 4-year period 1950–3, 841 had a diastolic blood pressure of 100 mm. Hg or higher, with minimal to severe signs and symptoms of hypertension. During the same period 564 (190 male and 374 female) out of 5,794 patients admitted to the wards were suffering from hypertension. Breathlessness and fatigue were the commonest symptoms, being present in 71% of the men and 81% of the women; 18% of the men and 27% of the women were admitted on account of cerebral vascular accidents. Following discharge from hospital information was obtained as to the progress of 77% of the patients. This showed that death had occurred in 47% of the men at an average interval of 19 months after discharge, and in 35% of the women after an average of 23 months. Cerebral vascular accidents accounted for 30% of deaths in females and for 19% in males. Heart failure was present in 44% of males and 35% of females; 13% of males and 14% of females had renal failure.

Having thus emphasized the frequency and importance of hypertension, the authors proceed to discuss in general terms its natural history and medical management.

K. G. Lowe

948. **Twenty Years' Experience with the Surgery of Hypertension**
E. A. KAHN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 633–638, Oct. 14, 1954. 14 refs.

In this paper the author re-asserts many of the difficulties inherent in assessing the place of sympathectomy in the management of arterial hypertension. There is still no method of forecasting the effect of the operation on the blood pressure, and the comparison of results from different clinics is valid only under certain stated conditions. In a series of 268 cases reported here which were operated upon by Peet between 1946 and 1949 bilateral supradiaphragmatic splanchnic neurectomy, including resection of the sympathetic trunks from D12 to D6 or higher, was performed in one stage. Of these patients, 65% were classified in Keith and Wagener's Groups 3 and 4 (poor prognosis for life). The death rate 5 to 8 years after operation was 22%, which compares favourably (within the limits stated) with the published results of thoracolumbar and near-total sympathectomy. A reduction in diastolic pressure of 20 mm. Hg or more occurred in 55% of the survivors (42% of the total), and this also compares favourably with the results of other varieties of sympathectomy.

The author discusses the possible dangers arising from sensory denervation of the upper abdominal viscera by splanchnic neurectomy. He also mentions that in 7 cases in which ligation of the thoracic duct was added to the sympathectomy no increased clinical benefit resulted, although several patients on whom a similar ligation was performed because of postoperative chylothorax had seemed to do particularly well. He concludes that in the absence of renal failure sympathectomy, followed if necessary by a medical regimen, is at present the most successful means of increasing life expectancy in patients with severe idiopathic arterial hypertension, and regrets that the procedure has not yet been accepted by the majority of physicians.

C. J. Longland

949. **The Treatment of Severe Hypertension**
M. L. ROSENHEIM. *British Medical Journal* [*Brit. med. J.*] **2**, 1181–1193, Nov. 20, 1954. 9 figs., bibliography.

Haematology

950. **Splenectomy, Cortisone, and Corticotrophin (ACTH) in the Treatment of Certain Blood Dyscrasias**
R. H. E. Elliott and G. A. Hyman. *Surgery* [*Surgery*] 36, 610–620, Sept., 1954. 44 refs.

The therapeutic value of splenectomy in certain blood dyscrasias is well established; treatment with adrenocortical hormones has been less uniformly successful. A review of the literature since 1950 shows that there have been few studies reported of the combined effects of splenectomy, cortisone, and corticotrophin (ACTH) in the treatment of these diseases. The present paper from the Presbyterian Hospital (Columbia University), New York, gives the results in 25 cases of such combined treatment and compares them with those in 21 similar cases treated by splenectomy alone without hormone therapy. The two groups included 14 and 8 cases respectively of thrombocytopenic purpura, 6 cases in each group of acquired haemolytic anaemia, and 12 miscellaneous cases of hypersplenism.

In none of the 25 cases treated with hormones pre- or post-operatively was there any instance of adrenal failure during or after operation, and there was no interference with wound healing. Of the 14 patients with thrombocytopenic purpura, cortisone or ACTH produced satisfactory remissions in 5 cases and symptomatic improvement in 5, while of the 6 cases of acquired haemolytic anaemia, beneficial results were obtained in 3 but no improvement in the other 3. In only one of the 5 cases of hypersplenism in this group was there any response to hormone therapy. The authors conclude from these results that in selected cases of thrombocytopenic purpura and acquired haemolytic anaemia cortisone and ACTH may be used with advantage as a means of preparing patients for splenectomy, and postoperatively in tiding them over a difficult period. *John F. Wilkinson*

951. **Homozygous Hemoglobin C. A New Hereditary Hemolytic Disease**
D. W. Terry, A. G. Motulsky, and C. E. Rath. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 365–373, Sept. 2, 1954. 11 figs., 24 refs.

The authors describe clinical, haematological, and genetic studies carried out at Georgetown University School of Medicine, Washington, D.C., on a patient with homozygous haemoglobin C. The findings were in general in agreement with those in 3 other cases of haemoglobin-C disease recently reported in the American literature. The authors' patient was a 44-year-old negress, and 13 close relatives, including 9 siblings, were available for the genetic study. Clinically, the patient complained of weakness and dyspnoea on exertion, and gave a history of intermittent arthralgia since childhood. The spleen was enlarged and palpable. Anaemia was mild (haemoglobin value 11·2 g. per 100 ml.) and of the normochromic, microcytic type. Reticulocytes formed between 2 and 3% of the erythrocytes. Examination of blood films showed numerous target cells (30%), and many erythrocytes very thin and folded, producing boat-shaped forms. The erythrocyte osmotic fragility was moderately decreased before incubation and became markedly so after incubating for 24 hours. Tests for sickling were repeatedly negative. Survival studies indicated that the mean life of the patient's erythrocytes in a normal recipient was shortened to 42 days. Electrophoretic studies showed 100% of the haemoglobin to be of Type C.

The approximate incidence of the haemoglobin-C trait (heterozygous form) in the negro population of the United States has been estimated to be 2·5%, so that the expected frequency of homozygous haemoglobin C may probably be about 1 in 6,000. The authors suggest that homozygous haemoglobin-C disease should be considered in all cases of unexplained anaemia, obscure arthralgia, or idiopathic splenomegaly in the negro. The differential diagnosis between haemoglobin-C disease and the various types of sickle-cell disease and thalassaemia is discussed. *J. V. Dacie*

952. **Anaemia of Pregnancy Treated with Intramuscular Iron**
J. M. Scott and A. D. T. Govan. *British Medical Journal* [*Brit. med. J.*] **2**, 1257–1259, Nov. 27, 1954. 4 figs., 11 refs.

At the Royal Maternity and Women's Hospital, Glasgow, 50 pregnant women with iron-deficiency anaemia were treated with a new carbohydrate–iron preparation, "imferon" [see Abstract 865]. All the patients had haemoglobin values of less than 10 g. per 100 ml. In 14 cases the anaemia was mild (9 to 9·5 g. Hb per 100 ml.), in 28 moderate (8 to 8·9 g. Hb per 100 ml.), and in 23 severe (haemoglobin value less than 8 g. per 100 ml.). In all but one case the erythrocyte count was over 3,000,000 per c.mm. The serum iron level, estimated by the method of Sven Dahl, was uniformly low (10 to 65 μg., average 35 μg., per 100 ml.). The first 13 patients were given daily injections equivalent to 100 mg. of elemental iron, but all subsequent patients received the equivalent of 250 mg. twice weekly. Daily estimations of the haemoglobin and haematocrit values and number of reticulocytes were made on those patients receiving a daily injection, and similar estimations were made at regular intervals on other patients. Each week a complete haematological investigation was made, and serial estimations of serum iron content carried out in selected cases.

There was a satisfactory response in all cases, the average weekly dose of 500 mg. of elemental iron producing an increase in haemoglobin level of slightly more than 1 g. per 100 ml.; the utilization of iron was good, the total haemoglobin level increasing on an average

by 0·3 g. for every 100 mg. of elemental iron injected. (These results are almost identical with those obtained from the intravenous administration of saccharated oxide of iron.) As with all forms of iron therapy response to treatment was sometimes delayed, but by the second week of treatment all patients showed similar increases in haemoglobin values. No local or general side-effects were noted in this series. As this preparation contains a higher concentration of elemental iron (50 mg. per ml.) than does saccharated oxide of iron (20 mg. per ml.) the number of injections necessary may be considerably reduced. *Robert Hodgkinson*

953. **A Study of Haemophilia. Presentation of Four New Cases of Haemophilia B (Christmas Disease, P.T.C. Deficiency).** (Étude sur l'hémophilie. Présentation de quatre nouveaux cas d'hémophilie B)
M. VERSTRAETE and J. VANDENBROUCKE. *Revue belge de pathologie et de médecine expérimentale* [*Rev. belge Path.*] **23**, 208–236, Aug., 1954. 3 figs., 36 refs.

In reporting a detailed description of 4 fresh cases of Christmas disease seen at the University Medical Clinic, Louvain, the authors present an illuminating discussion of the three known varieties of haemophilia. The classic malady (haemophilia A) is characterized by a lack of antihaemophilic factor (A.H.F.), haemophilia B (Christmas disease) by a deficiency of Factor IX (plasma thromboplastin component; P.T.C.), while haemophilia C differs from the other two types in that the deficiency is of plasma thromboplastin antecedent (P.T.A.) and both males and females are affected. It has been shown that in cases of haemophilia B the addition of blood from a patient with haemophilia of Type A restores coagulation to normal *in vitro*.

Full technical and clinical details of the authors' cases are given [for which the original paper should be consulted]. The authors emphasize the following important points: (1) sporadic cases of haemophilia B are commoner than those of Type A; (2) although the main features of Types A and B are similar, articular haemorrhage is less common and less severe in Type B than in Type A; (3) the incidence of all forms of haemophilia is low, probably about one case in every 80 cases of haemorrhagic disorder; (4) it seems to have been conclusively shown that Factor IX is not purely an accelerator of the formation of thromboplastin—the fact that it is diminished in some but not all patients under treatment with dicoumarol poses some interesting problems. *A. Piney*

954. **A Critical Study of Monocytic Leukaemia.** (Étude critique des leucémies à monocytes)
R. DEGOS, B. OSSIPOWSKI, and H. BARANGER. *Presse médicale* [*Presse méd.*] **62**, 1441–1445, Oct. 27, 1954. 14 figs., 14 refs.

The authors recall that three types of monocytic leukaemia have been distinguished: (1) that described by Naegeli, in which the increase of monocytes is part of a myeloid leukaemia; (2) a type in which the proliferating cells are intermediate between monocytes and large lymphocytes; and (3) leukaemic reticulosis of the type described by Reschad and Schilling-Torgan. Four cases illustrative of these types are briefly described.

The second type is perhaps the most doubtful. In one of the cases cited the authors describe the lymphoid cells as being the size of small lymphocytes, with an indented nucleus of the Rieder type having distinct nucleoli. Such cells formed 70% of the leucocytes in the peripheral blood, and " monocytoid elements " 10%, whereas it is stated that in the marrow prolymphocytes or even lymphoblasts formed 34%, while 14% consisted of histomonocytic cells. Lymph-node puncture showed many abnormal reticular cells, with large numbers of nucleoli. [But there is no mention of monocytes and, in short, there is no certainty that this was not a case of acute lymphocytic leukaemia. This paper does not, therefore, throw any clear light on the old and vexed question of the nature of the monocyte and of monocytic leukaemia.] *A. Piney*

955. **Myeloid Metaplasia as a Sequela of Polycythemia**
E. STEINFIELD and L. H. BEIZER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 388–395, Oct., 1954. 1 fig., 16 refs.

The authors describe 2 cases of polycythaemia in which anaemia with myeloid metaplasia of the liver and spleen eventually developed. They refer to similar cases reported in the literature. *P. C. Reynell*

956. **An Analysis of the Direct Hydraulic Effect of Intra-arterial Transfusion**
C. M. SMYTHE, J. P. GILMORE, J. V. MALONEY, and S. W. HANDFORD. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 412–418, Sept., 1954. 3 figs., 22 refs.

In experiments carried out at the U.S. Naval Medical Field Research Laboratory, Camp Lejeune, North Carolina, in which dogs were given intra-arterial injections of blood for the treatment of oligaemic shock, it was found that the increase in pressure resulting from such a transfusion can be predicted with considerable accuracy by using a modified Poiseuille equation relating the rate of infusion to the peripheral resistance at the time of injection, the predicted pressures being generally higher than the observed. From their observations the authors conclude that the hydraulic effect of intra-arterial transfusion does not explain its clinical effectiveness in the treatment of certain forms of shock. They suggest that the rise in blood pressure often observed during intra-arterial blood transfusion in shocked patients who have not responded to intravenous transfusions may be related to the observation of Coles that arterial puncture causes widespread reflex venospasm in cases of shock accompanied by venorelaxation, resulting in the sudden return of large volumes of blood to the heart. *A. I. Suchett-Kaye*

957. **Two Rare Human Blood Group Antigens.** [In English]
M. VAN DER HART, H. BOSMAN, and J. J. VAN LOGHEM. *Vox sanguinis* [*Vox Sanguinis (Amst.)*] **4**, 108–116, Sept., 1954. 2 figs., 18 refs.

See also Venereal Diseases, Abstract 893.

Respiratory System

958. **Simple Spontaneous Pneumothorax**
J. A. MYERS. *Diseases of the Chest* [*Dis. Chest*] **26**, 420–441, Oct., 1954. 18 refs.

A review is presented of 115 cases of spontaneous pneumothorax which had been kept under observation for periods up to 29 years. Although the ages of patients ranged from 15 to 64 years, 73% were between 15 and 29. Males accounted for 85% of the cases, a preponderance frequently reported which has never been satisfactorily explained. The left pleura was involved in 64 cases, the right in 42, and both in 9.

Pain was the predominant symptom, and radiation into the arms was not infrequently reported. The results of clinical examination provided no new information. Radiology revealed pulmonary collapse of 50% or more of the lung tissue in 67% of cases. No fatalities occurred in this series, but the hazards of positive-pressure pneumothorax are stressed. Expansion was complete in less than 6 weeks in over 80% of cases, and aspiration of air in uncomplicated cases is not advised. Tension pneumothorax demands aspiration, and this is advised also for haemopneumothorax. Complete bed rest is not considered to be necessary.

In no case was there any evidence of coexisting pulmonary tuberculosis, although this developed subsequently in 3 cases. Of 100 cases followed up for more than 6 months, a single recurrence had occurred in 17 (on the same side in 15), and more than one recurrence in 12. *J. N. Harris-Jones*

LUNGS AND BRONCHI

959. **The Clinical Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Chronic Pulmonary Disease**
P. A. THEODOS. *Diseases of the Chest* [*Dis. Chest*] **26**, 394–407, Oct., 1954. 2 figs.

The value of treatment with intermittent positive-pressure breathing combined with the administration of aerosols of various antispasmodic drugs has been assessed at Jefferson Medical College Hospital, Philadelphia, in over 700 patients with anthracosilicosis, hypertrophic emphysema, pulmonary fibrosis and emphysema due to causes other than the inhalation of coal-dust, or other chronic lung diseases. Oxygen was delivered under a positive pressure of 20 cm. of water during inspiration, expiration occurring against atmospheric pressure, the gas being used at the same time to nebulize the bronchodilator drug. Each treatment lasted for 20 minutes and was repeated 4 times daily for 3 to 6 weeks. The results were assessed from reports of subjective improvement, from reduction of sputum volume and disappearance of rhonchi, and from determinations of the vital capacity and maximum breathing capacity.

It is claimed that " moderate " or " marked " improvement occurred in 81% of 483 miners with anthracosilicosis, in 82% of 88 patients with hypertrophic emphysema, and in 73% of 60 patients with pulmonary fibrosis and emphysema. Similarly gratifying results were obtained in patients with bronchiectasis and bronchial asthma. Of the whole series, 220 patients were subjected to pulmonary ventilation tests before and after treatment. These disclosed that treatment had resulted in an average increase in vital capacity of 15% and an average increase in maximum breathing capacity of 28%.

The introduction of oxygen under a positive pressure during inspiration is considered to improve pulmonary ventilation, particularly in the periphery of the lungs, while the subsequent increased expiratory gas flow tends to wash out carbon dioxide, thereby reducing respiratory acidosis; bronchial drainage is enhanced in the same way. Positive-pressure inspiration also increases the dissemination of therapeutic aerosols and, by improving blood-gas exchange, increases the degree of arterial oxygen saturation, while the increase in thoracic excursion improves the tone of the diaphragm and intercostal muscles. The only contraindications to this form of treatment appear to be spontaneous pneumothorax and active pulmonary tuberculosis. Antispasmodics with a pronounced pressor effect are to be avoided in the presence of cardiovascular disease.

[The results recorded, if only temporary, are striking, but would be more convincing if controls had been used. No mention is made of the presence of cor pulmonale in any case in this series, nor of the potential hazards of oxygen therapy in this condition.]
J. N. Harris-Jones

960. **Present Status of Aerosol Therapy with Proteolytic Enzymes: Studies on the Cytology of Bronchial Secretions**
W. HABEEB, H. G. REISER, F. DICK, and L. C. ROETTIG. *Diseases of the Chest* [*Dis. Chest*] **26**, 408–419, Oct., 1954. 8 figs., 1 ref.

The authors have extended the studies of aerosol therapy with proteolytic enzymes previously reported by Limber *et al.* (*J. Amer. med. Ass.*, 1952, **149**, 816; *Abstracts of World Medicine*, 1952, **12**, 532) and now report their observations during the treatment of 152 cases of pulmonary infection over a period of one year, using a solution of 125,000 units of trypsin in 2 ml. of Sorensen's phosphate buffer administered by means of a nebulizer twice a day. Of 45 cases of pulmonary tuberculosis treated, 43 showed definite improvement in that cough, toxicity, and the volume of sputum were all reduced. A reduction in bacterial count is also claimed. Trypsin therapy is considered to be ideal for diffuse bronchiectasis too advanced for surgery, and of 25 such cases treated, all showed improvement. In 9 cases of

postoperative atelectasis re-expansion followed trypsin treatment, occasionally after a single dose of 250,000 units. Unresolved pneumonitis due to a variety of organisms was treated in 6 cases, all of which are stated to have been improved or cured. Three patients with chronic lung abscess that had defied antibiotic and postural therapy recovered, with closure of the abscess cavity, after a course of trypsin inhalation. Temporary improvement was noted in 31 cases of spasmodic asthma during treatment, and of 29 cases of bronchitis with emphysema, pulmonary ventilation was improved in 24.

The authors consider that enzyme treatment might be of the greatest value for the cleansing and debridement of bronchiectatic and tuberculous lobes in preparation for surgical resection. They claim that most of the pyrexial and systemic reactions to the treatment can be controlled by the simultaneous use of antihistaminic drugs, and that local buccal and laryngeal soreness can be prevented by proper nebulization.

In a careful microscopical study of the sputum of 30 tuberculous patients receiving aerosol treatment in comparison with that of 30 similar patients not receiving such treatment they failed to find evidence that trypsin caused an increase in the number of metaplastic cells present, while histological sections of resected lobes from patients who had received courses of trypsin aerosol showed no evidence of metaplasia of the bronchial mucosa beyond that commonly associated with the disease process.

J. N. Harris-Jones

961. **The Effects of Pneumoperitoneum on Lung Function in Pulmonary Emphysema**
M. R. Becklake, H. I. Goldman, and M. McGregor. *Thorax* [*Thorax*] **9**, 222–225, Sept., 1954. 13 refs.

There have recently been several favourable reports of the treatment of emphysema by the induction of pneumoperitoneum. Claims have been made that by this procedure vital capacity, maximum breathing capacity, intrapulmonary mixing efficiency, residual volume, and arterial oxygen saturation on exercise have all been improved, and also that clinical improvement has usually run parallel. The present authors express some doubt as to the validity of these claims on the ground that the comparison has usually been based on lung function tests made on 2 occasions only, namely, before and during treatment. In view of the well-known fluctuation in severity of symptoms of emphysema and the observed wide range in the results of lung function tests, they stress the necessity of repeating the tests as frequently as possible before, during, and also after treatment.

In a study carried out by the authors at Johannesburg General Hospital, South Africa, on 11 patients with chronic hypertrophic emphysema the patient's vital capacity, maximum breathing capacity, residual volume, total lung capacity, oxygen saturation at rest and after exercise, and gas mixing index were assessed on numerous occasions before and after the induction of pneumoperitoneum (which was maintained for a mean period of 13 weeks). Only one patient showed significant improvement in more than 2 tests; 2 patients improved in 2 tests only, and one showed definite deterioration. A number of patients reported symptomatic, subjective improvement, but this did not tally with the contrary objective evidence provided by the tests. The authors conclude that pneumoperitoneum is not noticeably of value in severe chronic hypertrophic emphysema, but agree with Zak and Southwell (*Acta med. scand.*, 1953, **147**, 79) that it may be of some use in milder cases.

Ronald S. McNeill

962. **Respiratory Acidosis in Patients with Emphysema**
J. E. Cohn, D. G. Carroll, and R. L. Riley. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 447–463, Oct., 1954. 9 figs., 18 refs.

At Johns Hopkins University Hospital, Baltimore, 8 emphysematous patients, 5 with acute respiratory acidosis and 3 with chronic acidosis, were studied. The physiological mechanisms concerned in the production of acidosis and the clinical appearances are considered. In the acute cases pulmonary infection and acute heart failure were superimposed, and in the chronic cases cor pulmonale was present.

Treatment, which included administration of bronchodilator drugs, antibiotics, and oxygen and breathing exercises or the use of mechanical respirators, was successful in reversing the acid–base abnormality in the acute cases but not in the patients with chronic carbon dioxide retention. It is pointed out that the main dilemma in the treatment of these cases consists in the fact that the patient suffers from both hypoxia and hypercapnia, and that treatment of the former with conventional oxygen therapy increases the severity of the latter.

H. E. Holling

963. **Respiratory Acidosis. I. Effects of Decreasing Respiratory Minute Volume in Patients with Severe Chronic Pulmonary Emphysema, with Specific Reference to Oxygen, Morphine and Barbiturates**
R. H. Wilson, W. Hoseth, and M. E. Dempsey. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 464–470, Oct., 1954. 6 figs., 18 refs.

As a contribution to the study of respiratory acidosis, in particular the effect of removing the hypoxic stimulus to respiration, the authors, working at the University of Texas, have made observations on 26 patients with pulmonary emphysema while breathing first room air and then 99·6% oxygen for 20 minutes, the respiratory minute volume and the respiratory quotient being measured and the oxygen and carbon dioxide content and *p*H of the arterial blood determined. Mixed venous blood was obtained by cardiac catheterization. The effective alveolar ventilation was calculated from the standard formula (*Fed. Proc.*, 1950, **9**, 602). In addition, observations were made on 5 patients with cardiac failure and emphysema who had been treated with morphine and on another 5 patients with emphysema but without heart disease who had been given barbiturates for insomnia.

In the 26 patients breathing 99·6% oxygen the respiratory minute volume and effective alveolar ventilation were both significantly reduced. Subsequently the car-

bon dioxide tension in the alveoli was raised and the *p*H of the blood depressed. Thus removal of the hypoxic stimulus may result in uncompensated respiratory acidosis and in severe cases in coma. From their observations on the patients given morphine or barbiturates the authors conclude that these drugs, even in small doses, may so depress minute volume and effective alveolar ventilation in patients with pulmonary emphysema that there is grave danger of producing respiratory acidosis.

H. E. Holling

964. **A Physiologic Evaluation of the Effects of Diaphragmatic Breathing Training in Patients with Chronic Pulmonary Emphysema**
W. F. MILLER. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 471–477, Oct., 1954. 1 fig., 17 refs.

In an objective study carried out at the University of Texas Southwestern Medical School, Dallas, of the value of training in diaphragmatic breathing the pulmonary function of 24 patients with chronic pulmonary emphysema, in most cases associated with chronic bronchitis, was investigated before and after a 6- to 8-week period of such training. In all cases the training was instituted only after maximum improvement had been achieved by conventional measures. Diaphragmatic excursion was measured fluoroscopically; other methods and procedures are described in detail.

The results showed that diaphragmatic breathing produced a striking increase in tidal volume at a lower respiratory rate, a lowering of the respiratory midposition, and more effective alveolar ventilation, with increased arterial oxygen saturation and decreased carbon dioxide concentration. There was no significant increase in total ventilation, except when this had been initially diminished. The author concludes that training in diaphragmatic breathing produced improvement in pulmonary function, and that this is associated in many cases with a more effective cough mechanism, resulting in better evacuation of bronchial secretions.

H. E. Holling

965. **The Successful Treatment of Diseases of the Respiratory Tract by Continuous Postural Drainage and the Prevention Thereby of Recurrent and Chronic Affections**
L. B. ELWELL. *Diseases of the Chest* [*Dis. Chest*] **26**, 338–348, Sept., 1954. 5 figs., 8 refs.

In the author's opinion, most cases of recrudescence of respiratory disease owe their origin to the incomplete resolution of an initial lesion, a residuum of bronchial secretion persisting and becoming reinfected. For this reason he has treated recurrent cases of such diseases as pneumonia, bronchopneumonia, and bronchitis by continuous postural drainage. The patient is nursed on a bed the foot of which has been raised 18 inches (45 cm.) —that is, at an angle of 14½ degrees—care being taken to ensure that the mattress does not sag. If the sinuses are involved, no pillow is allowed. The patient's position is changed according to the degree of involvement of the various lobes. All the 599 patients treated in this way during 1952 were kept in this posture continuously during the night and for as long as possible during the day.

The author claims that painful pleurisy accompanied by excessive cough was dramatically relieved; many patients who were subject to repeated lower respiratory infections also received considerable benefit from the prophylactic point of view. Even in asthmatics the frequency of the attacks was lessened. Few failures are reported. A number of cases of facial oedema lasting for several hours after the patient rose were noted, but this soon regressed. Several patients aged over 60 are said to have tolerated the regimen well. On the whole the author appears to be optimistic about obtaining the patient's co-operation in this rather irksome therapy.

Photographs of patients undergoing the treatment are reproduced.

Paul B. Woolley

966. **The Differential Diagnosis of Non-specific Chronic Pneumonitis.** (Zur Differentialdiagnose der nicht spezifischen chronischen Pneumonitis)
W. RUBE. *Tuberkulosearzt* [*Tuberkulosearzt*] **8**, 668–675, Nov., 1954. 6 figs., 15 refs.

967. **Carcinoma of the Lung. A Report of 403 Cases**
D. P. BOYD, M. I. SMEDAL, H. B. KIRTLAND, G. E. KELLEY, and J. G. TRUMP. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 392–411, Oct., 1954. 7 figs., 3 refs.

A detailed study is presented of 403 cases (350 males and 53 females) of carcinoma of the lung; all the cases were seen at the Lahey Clinic, Boston, 159 before 1948 and 244 between January, 1948, and December, 1952. The difficulties of early diagnosis are stressed, the authors having found that symptoms had been present for more than a year in over 25% of the cases. Carcinoma was diagnosed radiologically in 364 of the cases, the diagnosis being confirmed by bronchoscopy in 193 out of 312 cases, by examination of a biopsy specimen in 132 out of 184 cases, and by examination of the sputum in 59 out of 117 cases. In 104 cases resection was performed, including lobectomy in 32, the operation being considered curative in 96 cases and palliative in 8. The operative mortality was 7·6%. The average duration of life of all patients was 10·7 months; of those treated medically it was 4·2 months and of those given *x*-ray therapy 7·9 months. The average duration of life of those operated on was 23·3 months after pneumonectomy and 32·5 months after lobectomy. The authors state that the number of patients who survived for more than 5 years was 15, or "37·8% of those undergoing curative resection" [39 in 1948 or earlier]. The authors do not consider that the use of high-voltage radiotherapy made any considerable contribution to treatment, apart from giving symptomatic relief and acting as an adjuvant to surgery in certain cases.

[This comprehensive survey, which is accompanied by some excellent illustrations, should be read in its entirety by those interested.]

C. A. Jackson

968. **Triethylene Melamine in Bronchogenic Carcinoma with Vena Caval Obstruction**
M. SALINE and G. L. BAUM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1493–1495, Dec. 18, 1954. 1 fig., 9 refs.

Otorhinolaryngology

969. **Respiratory Mucosal Vascular Responses, Air Conditioning and Thermo-regulation**
P. COLE. *Journal of Laryngology and Otology* [*J. Laryng.*] **68**, 613–622, Sept., 1954. 2 figs., 11 refs.

The author has recorded the temperature of pernasally inspired air in the pharynx, of nasal expired air, and of the inferior turbinate submucosa, the subject breathing air of stable temperature and being exposed to the effect of intravenous vasodilators and of heat and cold applied so as to alter the temperature of the body or of some distant local part. From the results he concludes that the inferior turbinate is cooled by inspiratory air and its temperature is determined by the availability of blood-borne heat and the thermal demands of inspiratory air. When blood flow is decreased by a cooling stimulus to the body and inspiratory air is cold the turbinate mucosal temperature is low, and vice versa. Warm expiratory air before leaving the body comes into contact with this area of cooled mucosa, which, particularly if it is a large and complex area as in the dog, effectively extracts heat and water from the air before it leaves the anterior nares. Both factors—cold inspiratory air and decreased turbinate blood flow—contribute to heat conservation, which is much more marked with the large, complex type of turbinate. The inferior turbinate is thus a thermo-regulatory organ exercising its effect by controlling the condition of the expired air, the more effectively the more complex its structure.

T. A. Clarke

970. **The Conductive Mechanism of Hearing and Recruitment**
D. M. MARKLE. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **60**, 453–458, Oct., 1954. 5 figs., 1 ref.

If the hair cells, which are the end-organs of hearing, are contained in a fluid and sound is transmitted through air, the function of the middle ear must be that of a transformer—an impedance-matching mechanism. On this supposition the fluids of the inner ear, which convey sound waves to the hair cells, should be regarded as part of the conduction mechanism. It is believed that the presence of recruitment indicates a lesion within the neural mechanism of the ear; but recent work suggests that it occurs only when the hair cells are affected, not being found in retrocochlear lesions such as acoustic tumours, pontine-angle lesions, or presbyacusis. The present author suggests that recruitment is really not an indication of any type of nerve lesion, but is due to a conductive lesion within the cochlea. In an ear easily susceptible to noise, exposure to high-intensity sound causes a shift of the threshold which is reversible after rest. The threshold change affects bone conduction as well as air conduction, and the author finds that during the period of fatigue recruitment is present. In Ménière's disease, which is regarded as due to increased intralabyrinthine pressure, there must be increased impedance in the inner ear, and the author describes a case in which there was complete recruitment an hour before an attack of Ménière's disease and return of hearing without any recruitment 15 hours later. In another case a patient had a clinically typical unilateral nerve deafness with recruitment, tinnitus, and loss of discrimination. In spite of the otological findings, as the patient complained of continued " stuffiness " in the ear, myringotomy was performed empirically. There was a sensation of air rushing in, and 2 hours later the deafness and the recruitment had gone. The author suggests that negative pressure in the middle ear caused a bulge of the round-window membrane, lowering perilymph pressure as against endolymph pressure and so producing a " Ménière " effect on the membranous labyrinth.

Lowering of bone conduction may be due to fixation of the windows with an " impedance mismatch " between the oval and round windows, and the same may occur in adhesive otitis. In such cases it is difficult to estimate how much of the bone-conduction loss is really due to nerve degeneration; here the presence or absence of recruitment is important.

[Many years ago Mygind laid down that the fluids are part of the conduction mechanism. The finding reported here that reversible recruitment occurs in fatigue requires confirmation.] *F. W. Watkyn-Thomas*

971. **Inner Ear Pathology Due to Measles**
J. R. LINDSAY and W. G. HEMENWAY. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. [St. Louis)*] **63**, 754–771, Sept., 1954. 9 figs., 22 refs.

Although the examination of deaf children has shown that deafness may be due to the direct effect of the virus of measles on the inner ear, causing a neurolabyrinthitis or acoustic neuritis, few accounts have been given of the pathology in such cases. The present authors describe the findings at necropsy on a male infant aged 7 months who died from bronchopneumonia following measles. Evidence of a direct effect of the virus on the sensory cells of the cochlea was found on microscopical examination; the damage affected chiefly the stria vascularis, but degeneration of Corti's organ occurred throughout. The change was more marked at the base of the cochlea than at the apex, and the vestibular labyrinth was only slightly affected, corresponding with the clinical observation that measles attacks the cochlea more often than the vestibular apparatus. *William McKenzie*

972. **The Intranasal Use of Hydrocortisone Alcohol**
L. E. SILCOX. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **60**, 431–439, Oct., 1954. 13 refs.

The early enthusiasm for cortisone and corticotrophin (ACTH) in the treatment of allergic nasal conditions has been offset by the recognition of many disadvantages —these substances are not easily soluble in water, improvement is uncertain and often transitory, and

treatment may have objectionable, and even dangerous, side-effects. Hydrocortisone alcohol, which is more potent than cortisone or hydrocortisone acetate and much more soluble in water than either, was therefore substituted in a series of 174 cases which were observed for a year at the Graduate Hospital of the University of Pennsylvania, Philadelphia. There were 98 patients with allergic rhinitis, 57 with allergic rhinitis and polypi, and 19 with acute rhinitis. Whereas cortisone alcohol was ineffective in all conditions, hydrocortisone alcohol was effective in all cases except those of acute rhinitis, though the effect on polypi was " often dramatic but sometimes temporary ". The best results were obtained with a dilute solution of hydrocortisone alcohol (20 mg. per 100 ml.) containing 0·5% of hydroxyamphetamine hydrobromide and 0·125% of phenylephrine hydrochloride. In a further series of cases the antibiotics polymixin B, neomycin, and gramicidin (tyrothricin) were added to this last solution. With this, acute rhinitis was definitely improved, as were cases where infection was associated with the allergic state. The author explains the action of these substances thus: the pituitary hormone corticotrophin stimulates the production by the adrenal cortex of steroids which modify inflammatory reaction and minimize the allergic signs of hypersensitivity; they also neutralize the hyaluronidase released in allergic inflammation and so limit the oedema.

F. W. Watkyn-Thomas

973. **Eosinophilic Granuloma of the Frontal Bone. Report of a Case**

B. H. SHUSTER and T. F. FLYNN. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 501–504, Oct., 1954. 5 figs., 4 refs.

Eosinophilic granuloma, a disease of the reticuloendothelial system, is related to Hand–Schüller–Christian disease and Letterer–Siwe disease, all three being regarded by some authorities as clinical gradations of the same disorder. Although no specific organism has been discovered, it is now thought that eosinophilic granuloma is infective in nature. Clinically, there is a non-tender enlargement of, or swelling over, the affected bone, with osteolytic changes on radiography. Histologically, clumps of eosinophils predominate, with plasma cells, reticular network, multinucleated giant cells, leucocytes, lymphocytes, and products of destruction and repair.

The case is described of a girl of 3 who was struck with a stick on the right forehead, causing minimal bleeding and two small abrasions. A few hours after the injury swelling of the right eyelid was seen, which in 2 days extended above the eyebrow; it was inflamed and tender but not very painful. A month later the swelling had increased and the eye was closed. The condition was regarded as due to osteomyelitis, but on exploration tissue apparently of a neoplastic nature was discovered. On microscopical examination the diagnosis of eosinophilic granuloma was made. Apart from *x*-ray evidence of irregular bony destruction all findings were negative. It was suspected that infection was superimposed on the granuloma and surgical removal was carried out. A large mass of yellow-brown tissue, apparently encapsulated and with a minimal amount of purulent material, was found and removed. An area of dura covered with granulations was found exposed in the orbital roof. Recovery was complete and uneventful, and there has been no recurrence. The authors consider that in such a case surgery is better than radiation treatment, as adequate drainage can be established.

F. W. Watkyn-Thomas

974. **Rhinoscleroma Successfully Treated with Oxytetracycline (Terramycin)**

T. W. FOLBRE, L. MANHOFF, and D. W. FRAZIER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 505–507, Oct., 1954. 4 refs.

The authors describe what appears to be the first recorded case of rhinoscleroma successfully treated with oxytetracycline. The drug was given by mouth and, apart from the opening and dilatation of a stenosed nostril, no surgery was employed. The result supports the opinion that rhinoscleroma is caused by the von Frisch bacillus (*Klebsiella rhinoscleromatis*), one of the Friedländer group. Another interesting point is that the *Klebsiella* of granuloma inguinale, although attacking very different tissues, produces a histological reaction almost identical with that of rhinoscleroma and also responds to oxytetracycline. The patient, a woman of 66, had had a " sore " in the nose 6 years before treatment started. The right nostril was stenosed and the left filled with a granulomatous mass. The palate was scarred and bulged, the uvula was absent, and there was a smaller mass in the pharynx. Diagnosis was confirmed by histological examination and *K. rhinoscleromatis* was isolated. The patient was treated with 250 mg. of oxytetracycline hydrochloride 4 times daily for 3 weeks, followed by 250 mg. 3 times a day for a further 2 weeks. At the end of this period cultures were negative and Mikulicz cells much reduced in number. The stenosed nostril was split and a rubber splint worn for 4 weeks. On examination 14 months after treatment was started the patient was symptom-free, and nothing remained of the disease except scars on the palate, pharynx, and nostrils. There was normal ventilation through both nostrils.

F. W. Watkyn-Thomas

975. **Aureomycin Therapy in Laryngoscleroma. A Report on Five Cases**

A. EL-HAKEEM, E. EL-SAMMA, and I. MOSSALLAM. *Journal of Laryngology and Otology* [*J. Laryng.*] **68**, 523–534, Aug., 1954. 16 figs.

The natural history of scleroma as it affects the larynx is well known, and laryngeal obstruction has been observed in the atrophic, the nodular, and the cicatricial stages, but hitherto no definite line of successful treatment has been found. This paper from the Abbassia Faculty of Medicine, Cairo, records a series of 5 cases in which various antibiotics were used, aureomycin being strikingly successful in all in a dosage of one capsule (250 mg.) every 6 hours. The shortest course was 18 days, and the longest 37 days. No gastrointestinal complications occurred despite these long periods of aureomycin therapy.

S. A. Beards

Urogenital System

976. **Renal Hemodynamics during Erect Lordosis in Normal Man and Subjects with Orthostatic Proteinuria**
S. E. KING and D. S. BALDWIN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 634–636, Aug.–Sept., 1954. 10 refs.

Observations are reported from the U.S. Army Hospital, Fort Jay, New York, on the renal function in recumbency and erect lordosis of 5 normal subjects and of 5 others suffering from orthostatic proteinuria. Inulin and PAH clearances were determined in both postures, and in all cases the values fell to a similar extent when the erect lordotic position was assumed. It is concluded that " the rate of protein excretion in orthostatic proteinuria is not related to the magnitude of hemodynamic change occurring with erect lordosis ". *G. Loewi*

977. **Renal Papillary Necrosis: a Clinico-pathologic Study**
R. A. GARRETT, M. S. NORRIS, and F. VELLIOS. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 609–617, Oct., 1954. 6 figs., 11 refs.

During the past 10 years the authors, working at Indiana University Medical Center, Indianapolis, have observed 6 patients with renal papillary necrosis. All were female and their ages ranged from 21 to 78 years. Five were diabetic, their daily insulin requirements varying from 13 to 80 units. All had dysuria, haematuria, chills, fever, nausea, and vomiting, and were regarded as having pyelonephritis; 2 were in coma. In 4 cases the course was rapidly fatal, and the presumptive diagnosis of renal papillary necrosis was confirmed at necropsy.

One case is reported in detail—that of a 43-year-old woman with hypertension and diabetes who had been treated for recurrent pyelonephritis. She developed haematuria and passed per urethram a piece of tissue recognizable on histological examination as a necrotic papilla. Retrograde pyelography showed such changes as " ring shadow " (due to a sloughed papilla lying in a calyx) and clubbed minor calyces. She made a good recovery with multiple antibiotic therapy. A subsequent attack of right renal colic was relieved by ureteric catheterization, since when she has remained symptom-free. *K. G. Lowe*

978. **Excess of Vasopressor Activity in Plasma of Nephritic Children with Hypertension**
G. C. ARNEIL and J. B. DEKANSKI. *Lancet* [*Lancet*] **2**, 1204–1207, Dec. 11, 1954. 4 figs., 10 refs.

In an attempt to solve the problem of whether the transient arterial hypertension observed at the onset of acute haemorrhagic nephritis in children could be due to the presence of pressor substances in the blood, the authors tested the plasma of 8 children in the early stages of acute glomerular nephritis but with no history or evidence of previous renal disease for the presence of pressor activity, using Dekanski's method for estimating the pressor effect on the blood pressure of the rat (*Brit. J. Pharmacol.*, 1951, **6**, 351, and 1954, **9**, 187). Plasma from a healthy individual caused no rise in the rat's blood pressure, whereas plasma from the patients with acute nephritis increased the blood pressure noticeably, and still more if the plasma had been kept in an incubator for 12 hours at 37° C. The effect of injections of plasma in increasing doses was compared with the effect of injections of hypertensin (angiotonin) of known concentration, permitting quantitative comparison of the pressor activity of the two substances and assessment of pressor unit per 100 ml.

In the plasma of all 8 patients during the hypertensive phase of their illness the pressor activity was many times greater than after their recovery, when it returned to nearly normal levels. The authors confirmed that the pressor activity of the patients' plasma was not due to adrenaline, noradrenaline, *iso*amylamine, tyramine, pyridine, or nicotine, nor to pituitary vasopressin; the substance, whatever it may be, behaves like hypertensin, with which it may be identical. *L. H. Worth*

979. **Electrophoretic Studies of the Nephrotic Syndrome in Children: Preliminary Report**
G. B. STICKLER, E. C. BURKE, and B. F. MCKENZIE. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 555–561, Oct. 13, 1954. 3 figs., 17 refs.

The changes in the pattern of the serum and urinary proteins of 10 children with the nephrotic syndrome and marked oedema were studied at the Mayo Clinic by both the Tiselius and paper electrophoretic methods. In all cases the serum showed a decrease in albumin fraction to a mean of about 15% of the total protein (instead of the normal 59%), an increase in α_2 globulin to a mean of 46% (instead of about 10%) and in β globulin to a mean of 31% (instead of 15%), with incomplete separation of the two fractions in 2 cases, and a diminution or absence of γ globulin (3% instead of 12%). The urinary proteins showed a relatively high albumin content (66% of total protein) and the α_2 globulin content was 4·5%.

In 4 of the cases which were treated with 150 mg. of corticotrophin per sq. metre of body surface per day for 10 days there was good diuresis and marked clinical improvement at the end of treatment; but, in contrast to the observation of Farnsworth and Ruppenthal (*J. Lab. clin. Med.*, 1951, **38**, 407), the abnormal electrophoretic pattern in these patients showed only a partial return to normal. Various possible causes of the reduction in the serum and urinary α_1 and γ globulin values during the nephrotic syndrome and the prognostic significance of the serum electrophoretic pattern after diuresis are discussed. *J. E. Page*

Endocrinology

980. **Renal Disease in Hyperparathyroidism**
A. D. MORGAN and N. F. MACLAGAN. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 1141–1167, Nov.–Dec., 1954. 17 figs., bibliography.

To illustrate the interrelation between renal disease, hyperparathyroidism, and osteitis fibrosa, 3 cases of hyperparathyroidism seen at the Westminster Hospital, London, are described and illustrated, 2 being secondary to chronic pyelonephritis and one to a primary parathyroid adenoma. The authors conclude that there is no marked anatomical or histological difference between the primary parathyroid adenoma and some forms of secondary hyperplasia, nor do the findings in the kidneys differ greatly in the two conditions. The occurrence of metastatic calcification appears to be associated with a rise in the solubility product for calcium phosphate in the serum, and the authors found that the use of the serum ionized calcium level, as derived from the total serum calcium and protein levels with the nomogram of McLean and Hastings, in the calculation of this product gave closer correlation with the clinical findings than the use of the total serum calcium level itself. The main differential biochemical criteria between primary and secondary hyperparathyroidism are that in the latter the serum phosphate level is increased and urinary excretion of calcium is reduced, whereas in the former the serum phosphate level is low and urinary calcium output high; this difference in calcium excretion is particularly useful as it persists even in advanced cases, whereas the blood changes may become distorted.

J. B. Enticknap

PITUITARY GLAND

981. **Incomplete Pituitary Insufficiency. An Essay in Diagnosis**
L. A. WILSON, W. H. R. AULD, and W. BOWMAN. *Lancet* [*Lancet*] **2**, 715–720, Oct. 9, 1954. 2 figs., 34 refs.

In this paper from Aberdeen General Hospitals and the University of Aberdeen the authors discuss the difficulties associated with diagnosis of incomplete pituitary insufficiency, and describe the symptoms and biochemical findings in 8 cases (7 of them in females). While intolerance of cold and loss of sexual function are common symptoms, they are not invariably present, nor is genital atrophy a constant finding. In the authors' cases the laboratory tests of endocrine function included estimation of the basal metabolic rate (B.M.R.), the plasma cholesterol level, and the urinary excretion of 17-ketosteroids (values of 5 to 15 mg. per 24 hours in women and 10 to 20 mg. in men being regarded as normal), the Kepler water-excretion test, and the insulin tolerance test. Usually the B.M.R. was low, and in females the excretion of 17-ketosteroids was extremely low. In 7 cases there was a positive reaction to the Kepler test, but insulin sensitivity was normal.

Treatment consisted chiefly in administration of testosterone, which produced striking improvement in 7 of the cases.

D. G. Adamson

982. **Cushing's Syndrome. Six Cases Treated Surgically**
R. N. BECK, D. A. D. MONTGOMERY, and R. B. WELBOURN. *Lancet* [*Lancet*] **2**, 1140–1144, Dec. 4, 1954. 3 figs., 7 refs.

A brief account is given of the main clinical features and laboratory findings in 6 cases of Cushing's syndrome treated by subtotal adrenalectomy without mortality. Details of operative and postoperative management are given, with emphasis on the use of cortisone. Attention is drawn to a skin reaction which has proved a useful indicator of postoperative cortisone deficiency. The gratifying long-term results of therapy are reviewed.—[Authors' summary.]

983. **Conditioned Depression of the Formation and Secretion of Thyrotrophic Hormone by the Anterior Lobe of the Pituitary Gland in Rats.** (Условнорефлекторное снижение образования и выделения тиреотропного гормона передней доли гипофиза крыс)
Y. B. SKEBEL'SKAYA. *Бюллетень Экспериментальной Биологии и Медицины* [*Byull. eksper. Biol. Med.*] **38**, 6–10, Oct., 1954. 6 refs.

In experiments carried out at the All-Union Institute of Endocrinology, Moscow, a total of 135 mature male rats were divided into five groups which were treated as follows: (1) controls receiving daily injections of saline; (2) given daily injections of 20 μg. of thyroxine for 22 to 44 days; (3) in this group a conditioned reflex was developed, with injection of thyroxine as the unconditioned stimulus and injection of saline as the conditioned stimulus, reinforced by an accurately timed illumination of the injection chamber; (4) this group was treated in the same way as Group 3, but the reinforcement was omitted; and (5) this group received injections of thyroxine, but the illumination of the chamber, to which the rats in Group 2 were subjected, was omitted. At the end of the experimental period, the thyrotrophic activity of suspensions of pituitary tissue from each group was assayed biologically by determining their effect on the weight and histology of the thyroid gland in chicks.

Tissue from rats of Group 1 produced a two- to three-fold increase in weight of the thyroid gland, whereas tissue from thyroxine-treated rats (Groups 2 and 5) produced no significant change, indicating a reduced secretion of thyrotrophic hormone. A similar reduction in secretion was found in tissue from rats of Group 3, but not in that from rats of Group 4, showing that this

conditioned reflex, like many others, requires reinforcement for its perpetuation. It is claimed that the possibility of a conditioned depression of thyrotrophic activity has thus been demonstrated. *A. Swan*

THYROID GLAND

984. **Thyrotoxic Periodic Paralysis**
E. G. ROBERTSON. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 182–188, Aug., 1954. 3 figs., 11 refs.

The symptomatology in 4 cases of periodic paralysis seen at the Royal Melbourne Hospital, Melbourne, is described. The patients were men aged 29 to 45 years and in all 4 the thyroid gland was implicated. In 2 cases there was the classic picture of exophthalmic goitre with marked hyperthyroidism; in the third, exophthalmic ophthalmoplegia was present with doubtful signs of hyperthyroidism; while in the fourth there was mild hyperthyroidism, but examination of the thyroid after thyroidectomy showed a mild chronic thyroiditis of non-specific type.

The most characteristic feature was paralysis of the lower limbs, which manifested itself when the patient tried to rise from the sitting position and the severity of which was proportional to the duration of sitting. The author states that in severe attacks weakness of the arms and of the grip of the hand may develop. In 3 of the author's cases muscular symptoms disappeared after thyroidectomy. *D. G. Adamson*

985. **The Diagnosis and Mechanism of Hypothyroidism in Children as Studied by Means of Radioactive Iodine.** (Le diagnostic et le mécanisme de l'insuffisance thyroïdienne de l'enfant étudiés à la faveur des épreuves au radio-iode)
M. BERNHEIM and M. BERGER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 3575–3584, Oct. 22, 1954. 5 figs., 13 refs.

The authors studied the fixation of radioactive iodine (^{131}I) by the thyroid gland in (1) 7 patients aged 16 months to 25 years with congenital myxoedema and extreme thyroid deficiency, (2) 4 patients aged 10 months to 14 years with moderate hypothyroidism, and (3) 2 children aged 4 and 8 years respectively with mental and physical retardation (due to birth injury) and moderate hypothyroidism. In addition, the urinary excretion of ^{131}I was studied and the serum protein-bound ^{131}I level determined.

In each group of patients a different type of disturbance of iodine metabolism and thyroid function was found. In Group 1 there was no evidence of fixation of ^{131}I, urinary excretion of the whole dose took place within a few days, and no protein-bound ^{131}I was present in the serum. Group 2 was characterized by weak fixation of ^{131}I by the thyroid and by the presence of considerable quantities of protein-bound ^{131}I in the serum; these findings are interpreted as being due to the presence of fragments of functional thyroid tissue subject to extreme pituitary stimulation. The injection of thyrotrophic hormone in 2 cases of this type did not cause any appreciable change. In Group 3 there was a high degree of fixation of ^{131}I and large quantities of protein-bound ^{131}I were present in the serum, these findings being attributed to peripheral failure of utilization of endogenous thyroid hormone. This phenomenon was observed only in these 2 patients, who both had defects of the central nervous system in addition to hypothyroidism, and is being investigated further. *V. C. Medvei*

986. **Developments in the Use of Radioactive Iodine in the Diagnosis and Treatment of Diseases of the Thyroid Gland.** (Neue Ergebnisse der Anwendung von J^{131} in Diagnostik und Therapie von Schilddrüsenerkrankungen)
W. HORST. *Strahlentherapie* [*Strahlentherapie*] **94**, 169–190, 1954. 26 figs., 19 refs.

The author records his experience in the diagnosis and treatment of thyroid disease with radioactive iodine (^{131}I) at the University Hospital, Eppendorf, Hamburg. A two-phase diagnostic test was performed on over 3,000 patients, measurements of radioactivity over the thyroid gland being carried out 2, 24, and 48 hours after the administration of 30 to 60 μc. of ^{131}I (the "iodine phase"), followed by estimation of the plasma protein-bound ^{131}I level after 2 days ("thyroxine phase"). On repeated testing normal controls gave remarkably constant results, whereas the results from patients with thyroid disorders were extremely variable, indicating irregularity of thyroid function. The reliability of this test may be increased by giving an injection of 100 to 500 units of pituitary thyrotrophic hormone on each of 3 successive days beforehand. This is particularly useful when iodine uptake has been diminished by the administration of abnormal amounts of thyroxine in cases of obesity or of iodine in cases of simple goitre, the uptake of ^{131}I becoming normal after thyrotrophic hormone has been given. In primary myxoedema on the other hand thyrotrophic hormone has no such effect. With the combined method, the author claims a diagnostic reliability of 97%. ^{131}I was used for the determination of the position and size of the thyroid gland in the neck and in the mediastinum in 191 patients with thyroid carcinoma, toxic adenoma, thyroid aplasia, and recurrence of hyperthyroid conditions. Characteristic "iso-impulse charts" are reproduced which demonstrate the application and value of the method.

Out of a total of more than 300 patients treated with ^{131}I for hyperthyroidism, the results in 200 who had been followed up for 6 to 45 months are presented, it being claimed that the treatment was completely successful in 92%, which equals the best results of surgical treatment. The indications for such treatment were: (1) recurrence after subtotal thyroidectomy; (2) ineffective treatment with antithyroid drugs when there was no marked thyroid enlargement and the patient had refused an operation; (3) the presence of any local or general condition making surgery undesirable; and (4) severe hyperthyroidism of long standing in patients over 40 years of age. The author distinguishes a type of case with "limited hyperfunction", to which he attaches particular importance.

Out of 38 patients with metastasizing thyroid carcinoma, a satisfactory therapeutic result was obtained in 5 with ^{131}I. *V. C. Medvei*

987. **A Study of Nodular Goitre Using Radio-autography as the Main Method of Examination**

J. A. FORBES. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] 3, 138–145, May, 1954. 13 figs., 9 refs.

The author points out that autoradiography, by giving a better indication of the area of uptake of radioactive iodine (^{131}I) in the diseased thyroid gland, largely overcomes the deficiencies of earlier methods. At the Royal Melbourne Hospital he has examined the autoradiographs obtained from 19 patients with nodular goitre (including 11 cases of carcinoma) and from 30 carcinoma transplants in rats. Tracer doses of ^{131}I were given orally to the patients about 15 hours before thyroidectomy or biopsy; 200 to 300 μc. was given to those with carcinoma and 100 μc. to those with simple goitre. It was found that the uptake and storage of ^{131}I was confined to the vesicles, but was patchy, especially in pathological conditions. In 10 cases of carcinoma with metastases (and also in the carcinoma transplants in rats) the ^{131}I content of the tumour, whether differentiated or not, was much less than that of the surrounding normal tissue.

Localized thyroid nodules were then obtained at operation from 11 patients who had previously received a tracer dose of ^{131}I; in 2 of these cases carcinoma was co-existent. The nodules were distinguishable by their histological and autoradiographic characteristics, and fell into five types: (1) involutionary nodules with little evidence of storage of ^{131}I; (2) hyperplastic nodules with an uptake of ^{131}I in excess of normal tissue; (3) degenerating active nodules with viable tissue at the periphery and vesicles showing relatively normal uptake and storage; (4) inactive cellular nodules with scattered vesicles showing but slight storage; and (5) nodules typical of Hashimoto's disease (one case only), in which storage of ^{131}I was confined to the few surviving vesicles.

The author sums up as follows. The uptake and storage of ^{131}I is found only in tumours in which vesicles are present, and in these is confined to the vesicles. When thyrotoxicosis co-exists with carcinoma of the thyroid it arises in thyroid tissue not involved in new growth, although the amount of thyroxine secreted by well-differentiated carcinomatous tissue may be sufficient to prevent myxoedema after the thyroid gland is removed. The early recognition of thyroid carcinoma may be impossible on histological grounds alone, and the criteria for the differentiation of benign and malignant tumours are uncertain. The author therefore suggests that autoradiography has a place in diagnosis. Those nodules with normal or excessive uptake of ^{131}I are unlikely to be neoplastic, while those with little or no uptake may or may not be so. *Robert de Mowbray*

988. **The Anti-thyroid Action of *para*-Aminosalicylic Acid**

A. G. MACGREGOR and A. R. SOMNER. *Lancet* [*Lancet*] 2, 931–936, Nov. 6, 1954. 7 figs., 26 refs.

It has been known for some time that PAS, even when given in normal dosage, can produce clinical hypothyroidism, but the frequency with which this occurs is not precisely known. During the period January, 1952, to August, 1953, among 83 patients at Southfield Hospital, Edinburgh, receiving 20 g. of sodium PAS per day for at least 5 months, 20 developed an enlarged thyroid, although not all of these had definite clinical hypothyroidism. A further 9 cases were reported to the authors, making a total of 29 known cases in a comparatively small area. A majority of those affected tended to be in the younger age groups.

Investigation showed that in 2 patients without signs or symptoms of hypothyroidism and who were non-goitrous the rate of excretion of radioactive iodine (^{131}I) was normal, whereas in the affected cases the basal metabolic rate was low (often −20% or less) and the rate of excretion of ^{131}I high, implying poor usage of iodine by the thyroid gland in its depressed state. The administration of 4 to 8 grains (0·25 to 0·5 g.) of thyroid extract per day resulted in the goitre becoming smaller. It was noted that usually the blocking effect of PAS on the thyroid gland persisted only so long as the drug was being administered, but in one case the effect seemed to be permanent and in another examined at necropsy the histological pattern of the gland was grossly distorted. The authors suggest that thyroid medication should be given to all patients in whom a goitre is noted or to whom PAS is to be given for more than 6 months.

G. S. Crockett

989. **The Mechanism of the Goitrogenic Action of *p*-Aminosalicylic Acid**

D. A. W. EDWARDS, E. N. ROWLANDS, and W. R. TROTTER. *Lancet* [*Lancet*] 2, 1051–1052, Nov. 20, 1954. 3 figs., 10 refs.

It is well recognized that in some cases *p*-aminosalicylic acid (PAS) produces goitre with or without myxoedema. A strong indication that PAS exerts its goitrogenic effect by inhibiting hormone synthesis is given by the observation that the compound does not interfere with the iodine-concentrating mechanism of the salivary gland, although the two types of gland behave similarly with other antithyroid drugs.

The mechanism of action of PAS on the thyroid gland was therefore investigated by the authors at University College Hospital Medical School, London, in 2 thyrotoxic and 2 euthyroid patients who were given 200 mg. of methimazole by mouth in order to inhibit the organic binding of iodine. An hour later an oral tracer dose of radioactive iodine (^{131}I) was given, and the radioactivity in the neck and thigh was measured with a gamma counter at intervals. When the "thyroid count" (as determined by correction of the neck count for general tissue radiation) became steady 5 g. of sodium PAS was given by mouth. The thyroid count did not fall significantly in the next hour, indicating that the accumulated ^{131}I was retained and hence that PAS did not interfere with the concentrating mechanism. The ^{131}I was subsequently discharged by administration of potassium perchlorate, which does depress the capacity of the thyroid to accumulate iodine. In a further study 5 euthyroid patients who were being treated with sodium PAS for pulmonary tuberculosis were given an oral tracer dose of ^{131}I 1½ to 2 hours after the morning dose of PAS,

and then one hour later 200 mg. of potassium perchlorate to discharge the free iodine. The proportions of accumulated ^{131}I discharged in these cases were 25, 30, 75, 85, and 95% respectively, indicating that PAS is a moderate inhibitor of hormone synthesis.

The low incidence of goitre and myxoedema among patients receiving PAS is attributed partly to the relatively slight antithyroid effect of the drug and partly to its rapid rate of excretion (50% within 3 hours); in a few cases, however, the rate of elimination is slower, and hence the inhibition of hormone synthesis may be nearly complete. It is deduced from this work that PAS-induced goitre will be prevented by the administration of thyroid hormone, but not necessarily by giving iodides.

Nancy Gough

990. **Muscular Syndromes in Acquired Hypothyroidism in Adults.** (Les syndromes musculaires au cours de l'hypothyroïdie acquise de l'adulte)

—. GILBERT-DREYFUS, M. ZARA, and P. GALI. *Presse médicale* [*Presse méd.*] **62**, 1553–1554, Nov. 13, 1954.

The authors describe the muscular changes which were observed in 5 cases of hypothyroidism, in 3 of which they appeared after the treatment of hyperthyroidism with radioactive iodine. A review of the literature showed that such cases usually present with muscular pains and a pseudo-athletic muscular hypertrophy, with clinical and electrical evidence of myotonia, but occasionally there may be muscular atrophy. In the authors' cases recovery was rapid and permanent on treatment with small doses of thyroid extract. *F. W. Chattaway*

991. **Pigment : Creatinine Ratio in the Diagnosis of Thyroid Dysfunction**

G. J. FRIEDMAN, J. J. VORZIMER, H. R. MARCUS, E. DICKLER, W. V. TENZELL, A. GEFFEN, L. VENET, and I. FEUER. *Metabolism* [*Metabolism*] **3**, 518–522, Nov., 1954. 11 refs.

The clinical diagnosis of borderline cases of thyroid dysfunction is frequently difficult. Of the various laboratory tests, such as estimation of the basal metabolic rate (B.M.R.), serum protein-bound iodine level, and rate of radioactive iodine (^{131}I) excretion, employed as diagnostic aids, each is inaccurate or technically difficult and limited in its availability. In 1944 Ostow and Philo (*Amer. J. med. Sci.*, **207**, 507) showed that the urinary pigment : creatinine (P : C) ratio paralleled closely the basal metabolic rate of patients receiving thyroid extract. This method seemed to offer a simple and accurate measure of thyroid dysfunction, and the authors therefore further investigated it at Beth Israel Hospital, New York, by comparing the results of three tests of thyroid function, namely, determination of the B.M.R. by the respiratory-calorimeter method, of the urinary P : C ratio, and of the amount of ^{131}I excreted at 24 and 48 hours after administration of a standard dose; the tests were carried out simultaneously on 49 hyperthyroid, 77 euthyroid, and 3 hypothyroid patients.

The results showed that clinical diagnosis was confirmed by the B.M.R. test in 71% of the cases, the P : C ratio test in 76%, and the ^{131}I-excretion test in 84%. When the B.M.R. and P : C ratio test results were considered together agreement with the clinical findings was obtained in 94% of the cases.

The estimation of ^{131}I excretion was clearly the most accurate single test, but it is expensive and facilities for its performance are not widely available, whereas determination of both the B.M.R. and the P : C ratio is simple and cheap, and the combined results give even greater diagnostic accuracy. It is further suggested that serial determinations of the urinary P : C ratio would be particularly valuable in assessing the results achieved after the treatment of hyperthyroidism with antithyroid drugs or ^{131}I. *Nancy Gough*

ADRENAL GLANDS

992. **Cytological Demonstration of Noradrenaline in the Suprarenal Medulla under Conditions of Varied Secretory Activity**

N. A. HILLARP and B. HÖKFELT. *Endocrinology* [*Endocrinology*] **55**, 255–260, Sept., 1954. 1 fig., 11 refs.

The authors, working at the University of Lund and Karolinska Institute, Stockholm, have already shown that by oxidation of noradrenaline with potassium iodate *in vitro* a characteristic pigment is formed, and that this makes it possible to distinguish noradrenaline from adrenaline (*Acta physiol. Scand.*, 1953, **30**, 55). The present study was carried out on the adrenal medulla in varying states of secretory activity in an attempt to determine whether noradrenaline is formed at specific sites. In order to produce minimal secretory activity the adrenal medulla on one side was denervated in 4 cats, all nerves supplying the medulla being divided close to the adrenal gland. In the 21 rats observed the great splanchnic nerve on one side was cut immediately above its exit from the thorax. In both groups the opposite adrenal gland was preserved intact and served as a control. To obtain a condition of increased secretory activity in the medulla, in 8 cats and 16 rats hypoglycaemia of varying degree was induced by giving different doses of insulin acting for varying lengths of time. The animals were killed after 2 to 4 weeks and the adrenal medulla treated with potassium iodate to demonstrate the presence of noradrenaline and with potassium bichromate to demonstrate the simultaneous presence of noradrenaline and adrenaline. In a few cases quantitative estimations of the catechol amines were made colorimetrically.

It was shown that in both the cat and the rat the two oxidative procedures produced similar patterns in both the intact and denervated adrenal medulla. In the state of insulin-induced hypoglycaemia the adrenal medullary cells of both species showed a marked reduction of pigment formation when oxidized with potassium bichromate, the reduction being roughly proportional to the severity of the reaction. These results were confirmed by estimation of catechols. Since it is known that insulin-induced hypoglycaemia produces a reduction in the adrenaline content of the adrenal gland without any

decrease in the amount of noradrenaline, the authors conclude that the above results indicate that noradrenaline is formed by specific cell-complexes.

D. G. Adamson

993. **Experiments on the Existence of a Blood/Adrenal-cortex Barrier**

A. ELKELES. *Lancet* [*Lancet*] **2**, 1153–1154, Dec. 4, 1954. 12 refs.

The author of this paper from the Prince of Wales's and Metropolitan Hospitals, London, has extended his previous studies of the blood–brain barrier by an investigation of the vital-staining effects of acid and basic dyes on the adrenal glands and other tissues of the rabbit. This was undertaken in consequence of the observation that metastases in the brain from a renal carcinoma (the cells of which often resemble those of a tumour of the adrenal cortex) remained unstained like the cerebral tissue. For this purpose the basic dye neutral-red chloride, and the acid dyes "kiton fast green V", light green S.F., and phloxine were given intravenously in large doses and the animals killed 10 to 30 minutes after the injections. Macroscopical inspection of the organs and the tissues revealed that the acid dyes had stained the adrenal medulla and other tissues but not the adrenal cortex or the brain, whereas the basic dye stained the adrenal cortex and the brain but not the adrenal medulla or the other tissues.

The author concludes that the adrenal cortex and the brain react in the same way to vital staining and suggests that this is because the tissues of both organs, possibly on account of their lipid content, have an affinity for electropositively charged substances such as basic dyes, but not for electronegatively charged substances such as acid dyes. It is further suggested that the adrenal cortex may thus have an affinity for neurotropic toxins and viruses, which are electropositive, and that it may be necessary in future to consider the role of this vital organ in the causation of the pathological processes produced by these agents. It emerges from this study that the concept of a selective barrier confined solely to the endothelium of the cerebral capillaries is no longer tenable.

Charles Rolland

994. **Eosinopenia Induced by Stress in Adrenalectomized Dogs**

W. W. SWINGLE, M. EISLER, M. BEN, R. MAXWELL, C. BAKER, and S. J. LE BRIE. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 341–345, Aug., 1954. 3 figs., 21 refs.

Experiments are described which were carried out at Princeton University on dogs whose adrenal glands had been removed 1 to 4 years previously. They were being maintained on a daily dose of 0·5 mg. of deoxycortone acetate and a diet containing 0·70 to 0·85 g. of sodium and 0·58 to 0·75 g. of potassium daily, and the maximum spontaneous variation in the eosinophil count during the day was 25% (average 20·4%). Stress was applied in the form of the administration, without preliminary sedation, of sufficient ether to induce fright but not anaesthesia. If this stress was sufficiently prolonged it was followed within 2 to 5 hours by a striking fall in eosinophil count, the degree of which was proportional to the amount of muscular exertion caused by struggling. The eosinophil count also fell by 50 to 90% after stimulation with an electric current sufficient to induce fright but not pain or trauma.

Although the degree of stress required to induce eosinopenia in the absence of the adrenal glands was greater than that necessary in intact animals, the fact that so striking a fall in the eosinophil count could be induced suggests that factors other than C_{11}-oxysteroids from the adrenal cortex are concerned in this effect of stress. It is unlikely that accessory adrenal cortical tissue was present, since the withdrawal of deoxycortone was rapidly followed by symptoms of adrenal insufficiency. In view of the known effect of adrenaline in inducing a fall in the eosinophil count the possibility that the release of this substance from adrenergic nerve endings might be responsible for the phenomenon observed was considered. However, injection of the anti-adrenergic drug "regitine" in doses of 3 mg. per kg. body weight intramuscularly or of the anticholinergic drug "antrenyl" (oxyphenonium bromide) in the same dosage also caused a profound fall in the eosinophil count. Whereas antrenyl was toxic to the animals, regitine was not.

Robert de Mowbray

995. **Bilateral Subtotal Adrenalectomy for Cushing's Syndrome.** [In English]

C. A. HERNBERG. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **16**, 309–314, Aug., 1954. 10 refs.

Six patients with Cushing's syndrome due to adrenal hyperplasia were treated with subtotal bilateral adrenalectomy, performed in two stages at an interval of 2 to 4 months. Nine-tenths of both adrenals was removed. In one case complete adrenalectomy was performed on one side and a partial adrenalectomy on the other, three-quarters of the gland being removed. This was the only case with slight signs of recurrence 18 months after operation. In each case most of the symptoms typical of the syndrome disappeared. Three of the 5 female patients regained their menstrual periods, one became pregnant. In no case were there signs of adrenal insufficiency, but in one case there was marked darkening of the skin, probably due to hypophyseal overactivity. One patient died of an infectious disease 4 months after operation.—[Author's summary.]

996. **Use of Glycyrrhizin after Bilateral Adrenalectomy**

P. B. HUDSON, A. MITTELMAN, and M. PODBEREZEC. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 641–646, Oct. 14, 1954. 6 figs., 6 refs.

An evaluation of glycyrrhizinic acid for the maintenance therapy of patients subjected to bilateral adrenalectomy is reported from the Francis Delafield Hospital, New York. Three patients who had undergone bilateral adrenalectomy for metastatic cancer of various kinds were given a daily dose of 4 g. of ammoniated glycyrrhizin (*U.S.P.*) one to 3 months after the required minimum dose of cortisone had been established, cortisone being then progressively withdrawn. It was found

that the patients could not be maintained indefinitely on glycyrrhizin alone (one patient died from adrenal insufficiency), but they could be maintained for periods of several weeks on glycyrrhizin and a small dose (5 mg.) of cortisone. [The evidence that glycyrrhizin has a cortisone-like action seems suggestive only.]

G. A. Smart

997. **Clinical Investigation of Alleged Antagonism of Corticoids**

R. GOULDING, K. S. MACLEAN, and J. M. ROBSON. *Lancet* [*Lancet*] **2**, 775–777, Oct. 16, 1954. 1 fig., 6 refs.

The authors describe an experiment devised and carried out at Guy's Hospital, London, to test Selye's hypothesis that antagonism between the "mineralo-corticoids" (such as deoxycortone) and "glucocorticoids" (such as cortisone) is concerned in the pathogenesis of rheumatoid arthritis. For this purpose 8 patients with acute rheumatoid arthritis were admitted to the hospital, given a normal diet, and encouraged to be ambulant as far as possible, no treatment other than physiotherapy and the administration of steroids according to the following schedule being given. In the first week 1 ml. of sterile saline alone was given intramuscularly. Thereafter 100 mg. of cortisone was given intramuscularly each day, in addition to the saline, until a satisfactory remission was obtained, the dose being then reduced to the minimum maintenance level. At this point 20 mg. of deoxycortone acetate was next given each day in place of the saline (and in addition to the cortisone) for at least 7 days. In the final period of observation the maintenance dose of cortisone was given alone.

By the end of the first stage, while receiving cortisone alone, all 8 patients were in satisfactory, if incomplete, remission. No significant change in their condition occurred when deoxycortone was added, as judged by regular examination of the joints and determination of the fluid balance, body weight, blood pressure, erythrocyte sedimentation rate, eosinophil count, and serum sodium and potassium levels; nor was there any significant change when the deoxycortone was withdrawn and the cortisone continued.

From this admittedly small clinical trial the authors conclude that there is no evidence that deoxycortone exerts any adverse effect upon the protective action of cortisone in patients with rheumatoid arthritis. The possibility that other corticoids might have shown antagonistic action is briefly discussed, but is not considered very likely. *Robert de Mowbray*

998. **The Occurrence of Electrocortin in Human Urine**

C. L. COPE and J. GARCIA-LLAURADO. *British Medical Journal* [*Brit. med. J.*] **1**, 1290–1294, June 5, 1954. 5 figs., 18 refs.

Working at the Postgraduate Medical School of London, the authors have examined extracts of urine from 6 normal subjects, 4 patients with rheumatoid arthritis, and 3 with congestive heart failure for the presence of electrocortin, using a slight modification of the method of Tait *et al.*, who first described this adrenocortical steroid (*Lancet*, 1952, **1**, 122; *Abstracts of World Medicine*, 1952, **12**, 147). The method, which involves the use of adrenalectomized rats, is described in detail.

It was shown that a substance with sodium-retaining activity was present in small amounts in the urine of the normal subjects and of one of the 3 cardiac patients, but no trace of it was found in the urine of the rheumatoid arthritic patients. In all cases in which it was present the amount of sodium-retaining factor was very small, and several attempts to increase the output of this principle were made without success; for example, the urine of a normal subject maintained on a diet containing less than 0·5 g. of sodium daily did not show any increase of the sodium-retaining factor, nor did that of a patient maintained on doses of corticotrophin which were large enough to provoke a marked increase in hydrocortisone output. By chance the authors discovered a patient suffering from severe potassium loss associated with chronic pyelonephritis who, although in sodium balance, was found to be excreting large amounts of the sodium-retaining substance in the urine. The results of chromatographic analysis of extracts of her urine made it highly probable that this substance was electrocortin; thus a high titre of electrocortin in the urine does not necessarily imply a condition of sodium retention. The relation of rate of urinary excretion to blood level of the hormone is tentatively discussed, but too little is known as yet to permit of any definite conclusions.

Robert de Mowbray

PANCREAS

999. **Hyperglycemic and Glycogenolytic Activity of Preparations from Human Urine**

F. MOYA and M. M. HOFFMAN. *Endocrinology* [*Endocrinology*] **55**, 439–447, Oct., 1954. 3 figs., 17 refs.

A crude concentrate or an alcohol-insoluble fraction derived from the urine of normal men and women has consistently been found to be hyperglycemic and to induce an increased release of glucose by rabbit liver slices *in vitro*. Unlike pancreatic glucagon, the urinary factor is very active in stimulating glycogen breakdown in liver homogenates. It is concluded that the glycogenolytic activity of urinary preparations is at least partially due to a factor other than pancreatic glucagon. Uric acid, growth hormone, pitressin, adenosine-5-phosphoric acid and calcium ion failed to stimulate glycogenolysis in rabbit liver homogenates.—[Authors' summary.]

1000. **Circulatory Disturbances in the Retina in Diabetics.** (Durchblutungsstörungen der Netzhaut des Diabetikers)

E. HEINSIUS. *Klinische Monatsblätter für Augenheilkunde* [*Klin. Mbl. Augenheilk.*] **125**, 1–5, 1954. 10 refs.

The retinal vascular changes seen in diabetics may be grouped as follows. (1) Capillary disturbances, characterized by miliary aneurysms, petechiae, and patches of exudate, and occasionally by retinitis punctata; in their early stages these conditions do not affect the visual elements of the retina. (2) Arteriosclerotic disturbances, with changes in appearance of the arterial walls, con-

striction of the veins at crossings, irregularities of the arterial calibre, and patches of degeneration sometimes appearing as retinitis circinata. (3) Microscopic thromboses in the venous system of the retina or thrombosis of the central vein, leading finally to proliferating retinitis and blindness. This form of retinal change is less frequent than the first two. The differentiation of these forms is sometimes very difficult as they may be present simultaneously.

In treatment in such cases it is essential that the blood sugar level should be stabilized and septic foci cleared up. If retinal haemorrhages or aneurysms are present treatment with rutin, calcium, vitamin E (α-tocopherol), and male sex hormones is recommended. In the presence of general circulatory disturbances "priscol" (tolazoline), acetylcholine, and "padutin", given systematically or by retrobulbar injection, improve the vision in some cases. In 40 to 60% of cases the further progress of the disease may be halted, and in another 40% there is an improvement. *M. Klein*

1001. **The Retinopathy of Diabetic Vascular Disease.** (Die Retinopathie im Rahmen der diabetischen Angiopathie)
W. PÖRSTMANN and J. WIESE. *Klinische Monatsblätter für Augenheilkunde* [*Klin. Mbl. Augenheilk.*] **125**, 336–354, 1954. 10 figs., 33 refs.

In a study of 720 diabetic patients examined at the University Medical and Ophthalmological Clinics, Leipzig, between 1950 and 1952, retinopathy was present in 326 cases (45·3%). Four grades were recognized, ranging from Grade 1, in which yellowish-white foci of retinal degeneration which did not impair vision were observed, to Grade 4, the severest variety with an incidence of 1·7%, which was characterized by the presence of retinitis proliferans and was clearly associated with nephropathy. The average duration of the diabetes in those with retinopathy was 13 years, and retinopathy was twice as common in patients who became diabetic before the age of 45. The height of the blood pressure bore no relation to the grade of retinopathy, but arteriosclerotic vascular changes were common, 80% of cases with diabetic nephrosclerosis showing changes in the vessels of the fundi. *L. Cudkowicz*

1002. **Insulin Resistance following Hypothalamic Lesions and Removal of the Adrenal Medulla**
J. BEATTIE. *British Medical Journal* [*Brit. med. J.*] 1, 1287–1290, June 5, 1954. 13 refs.

After section of the pathways from the hypothalamus to the brain stem and removal of the adrenal medulla, rats kept at an environmental temperature of 29·5° C. showed no fall in the blood-glucose level 30 minutes after the injection of insulin in a dose of 1 unit per kg. body weight. Removal of the adrenal medulla alone or section of the hypothalamic pathways produced no change in insulin sensitivity.

The resting content of glycogen in muscle (gastrocnemius) was significantly lower than normal in rats with the hypothalamic lesions and without adrenal medullary tissue. The glycogen content did not rise after the injection of glucose (1 mg. per g. body weight) or after the simultaneous injection of glucose and insulin. The glycogen content of the liver was markedly reduced (15% of normal) in the resting state. When such rats were exposed to cold for 9 days they still displayed no hypoglycaemic response to the injection of insulin. The glycogen content of the liver in the resting state was reduced to 11 mg. per 100 g. of liver.

The experimental data suggest that the insulin resistance found in these rats was due to the presence of an insulin antagonist.—[Author's summary.]

1003. **Six-minute Test of Responsiveness to Insulin. Clinical and Preclinical Application**
G. E. ANDERSON. *Brooklyn Hospital Journal* [*Brooklyn Hosp. J.*] **12**, 5–19, 1954. 8 figs., 36 refs.

The author's six-minute test of responsiveness to insulin consists in the determination of the blood glucose level before, and at 2, 4, and 6 minutes after, the intravenous injection of 3 units of glucagon-free insulin (*Science*, 1954, **119**, 516). The author has carried out this test on 120 diabetic patients and 68 control subjects. In non-diabetic persons who are not obese a prompt fall in the blood glucose level by 6 to 26% of the fasting value occurs. Many obese non-diabetic subjects with a normal response to the glucose tolerance test were found to have a faulty response to insulin by the six-minute test, and it is suggested that such persons, especially if they have a family history of the disease, should be kept under careful dietary control as potential diabetics.

Diabetics could be divided into three groups according to the results of the six-minute test: (1) those with a poor response, typified by the obese adult diabetic before treatment, under inadequate treatment, or suffering from infection or some other factor breaking down diabetic control; (2) those normally responsive or overresponsive to insulin, such as the juvenile type of diabetic and the obese adult type under adequate control; and (3) the labile or "brittle" type in which bizarre and precipitous changes in the blood glucose level occur within the six-minute test period. It is claimed that the test serves as a more reliable index of clinical improvement or regression than casual blood glucose determinations.
K. O. Black

1004. **The Effect of *alpha*-Methyl Stilbene on Blood Sugar and on the Insulin Content of the Pancreas of Animals**
M. N. GREEN, S. B. BEASER, and A. M. SELIGMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 710–714, Nov., 1954. 14 refs.

Under the conditions of our experiments, the injection of alpha-methyl stilbene in olive oil subcutaneously into rabbits, rats, and dogs did not cause any change in the insulin content of the pancreas, contrary to results as previously reported by Griffiths. No changes were observed in the glucose tolerance curves of rabbits similarly treated who had been made either severely or mildly diabetic with alloxan.—[Authors' summary.]

See also Urogenital System, Abstract 977.

The Rheumatic Diseases

1005. **Rheumatic Pneumonia.** (Pneumonia Reumatica) I. NUSSENZVEIG, M. A. NOGUEIRA CARDOSO, E. PIMENTA DE CAMPOS, B. TRANCHESI, V. NUSSENZVEIG, and R. SONNTAG. *Archivos del Instituto de cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **24**, 55–89, Jan.–Feb., 1954. (Received Nov., 1954.) 15 figs., 48 refs.

In this paper from the University of São Paulo, Brazil, the authors review the extensive literature on rheumatic pneumonia, and point out that the difficulty has always been to decide whether rheumatic fever can give rise to a specific pneumonia or whether the pulmonary changes are secondary to heart failure. (Most workers admit the specificity of the changes.) They then report the findings in 10 fatal cases of rheumatic pneumonia confirmed at necropsy. In all cases there was active pancarditis. In most of them the onset of the pneumonia was sudden, and was characterized by rapid breathing, cyanosis, and restlessness, while sweating was frequently excessive. Physical signs in the lungs were always less than expected. The radiological signs were fleeting, areas of consolidation clearing up and then reappearing elsewhere. Post mortem the lungs were found to be of a rubber-like consistency; histologically the main changes were fibrinoid necrosis of the alveolar walls, with erythrocyte and mononuclear exudation, and hyaline degeneration of the interstitial tissue. In only one case were Aschoff nodes found in the affected tissue.

The onset of pneumonia in rheumatic fever aggravates the prognosis, and death usually occurs about the 9th day from respiratory failure. These cases occurred before ACTH was introduced, and all the drugs then available were found to be without effect.

Paul B. Woolley

1006. **A Study of the State of Vessel Permeability in Juvenile Rheumatism.** (К вопросу о состоянии сосудистой проницаемости при ревматизме у детей) O. D. SOKOLOVA-PONOMAREVA and V. P. BISYARINA. *Педиатрия* [*Pediatriya*] 3–6, No. 5, Sept.–Oct., 1954.

The authors consider that rheumatism is an infective–allergic illness in which at all stages functional and morphological changes occur in the blood capillaries. They report that in a study of 90 children suffering from acute rheumatic conditions, including 38 cases of joint disease, 32 of cardiac forms of rheumatism, and 20 of chorea, an annular rash was observed in one-third of the 46 children suffering from a first attack and in one-half of the 44 children having a second or subsequent attack. The capillary permeability was measured at least twice in each child by Landis's method (the number of leucocytes found in the tissue fluid expressed as a percentage of the total leucocyte count) and showed that: (1) a regular increase of capillary permeability was present in the active phase of all the forms of rheumatism studied, migration of leucocytes into the tissues occurring in 91% of the 90 cases; (2) in the joint and cardiac forms of rheumatism capillary permeability was increased by 5·3 to 6·5% in the first attack and still further increased (by 7·5 to 8·9%) in the second or subsequent attacks; in chorea, however, although capillary permeability was increased in the first attack (by 7·53%), in second or subsequent attacks it was decreased (by 4·76%); (3) improvement in the clinical state after a first attack of all the forms of rheumatism discussed was accompanied by a decrease in the capillary permeability, but in recovery from second or subsequent attacks (except of chorea) no such decrease in vessel permeability occurred with clinical improvement.

E. D. Fox

1007. **Vitamin A in Rheumatic Fever**
A. L. JACOBS, Z. A. LEITNER, T. MOORE, and I. M. SHARMAN. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **2**, 155–161, May–June, 1954. 2 figs., 7 refs.

The blood carotenoid and vitamin-A levels were studied in relation to body temperature and the erythrocyte sedimentation rate (E.S.R.) in 100 patients with acute rheumatism. For purposes of comparison similar observations were made on patients suffering from pneumonia, subacute rheumatism, pleural effusion, rheumatoid arthritis, erythema nodosum, and acute tonsillitis. A fall in the vitamin-A level was observed in association with a rise in temperature, but although there was general correlation, this inverse relationship did not always hold good in each individual case. Similarly there was a general tendency for the vitamin-A level to fall with a rise in the E.S.R., but the vitamin-A level did not fall as rapidly in rheumatoid arthritis with changes in the E.S.R. as it did in other conditions. A considerable fall in the blood vitamin-A level was observed in the 14 days preceding death, and also in the vitamin-A content of the liver in cases of heart disease due to rheumatic fever.

The authors are careful not to infer that rheumatic fever is different from any other infective process or that the changes in the vitamin-A level are in any way specific for rheumatic infections. They merely conclude that because the level is reduced in rheumatic fever daily administration of 40,000 to 50,000 international units of vitamin A is reasonable adjuvant therapy.

R. E. Tunbridge

1008. **Cortisone and Salicylates in Rheumatic Fever**
K. S. HOLT, R. S. ILLINGWORTH, J. LORBER, and J. RENDLE-SHORT. *Lancet* [*Lancet*] **2**, 1144–1148, Dec. 4, 1954. 1 fig., 9 refs.

A preliminary report is presented from the University of Sheffield on a controlled trial of cortisone and salicylates in high dosage in the treatment of rheumatic fever, which was carried out at the Children's Hospital, Sheffield, on 30 children ranging in age from 4 to 14 years. They were divided into three equal groups. Group 1 were given sodium salicylate in sufficient dosage to give a serum salicylate level of 30 to 40 mg. per 100 ml.,

the maximum daily dosage given being 150 grains (10 g.) per day. In addition this group received 200 mg. of cortisone by mouth daily at first, the dose being reduced in steps to 50 mg. a day in 5 weeks. Group 2 were given sodium salicylate alone, the dosage being adjusted to give the same blood salicylate level. Group 3 received a lower dosage of sodium salicylate (20 to 30 grains (1·3 to 2 g.) daily). In each group treatment was continued until the erythrocyte sedimentation rate (E.S.R.) was normal on three consecutive occasions at weekly intervals.

Only the effect on the E.S.R. is reported here; this rate fell significantly more rapidly when the drugs were used in combination than when salicylates were given alone either in high or low dosage, and the average duration of treatment, and therefore the period in hospital, was considerably shorter in Group 1 than in Groups 2 and 3.

[This is only a preliminary report on a small number of cases, but it comes from such an authoritative source that the findings must arouse considerable interest.]

Oswald Savage

1009. **Salicylates in Rheumatic Fever. Difficulties Experienced in Treating Children with Large Doses**

K. S. Holt. *Lancet* [*Lancet*] **2**, 1197–1199, Dec. 11, 1954. 3 figs., 19 refs.

Difficulties experienced in the treatment of rheumatic fever with large doses of salicylates are described. Between 1948 and 1954 a total of 52 children aged 4 to 14 years with rheumatic fever received 58 courses of salicylate, the dosage employed being sufficient to achieve a serum salicylate level of 30 to 40 mg. per 100 ml. In 12 of the courses cortisone was given in addition. Frequent adjustments (totalling 172) had to be made in the dosage to maintain the desired blood level. Toxic symptoms were common. Hyperpnoea occurred 30 times in 17 cases; on 18 occasions it was the only toxic symptom; on 5 occasions it was associated with vertigo, on 4 with drowsiness, on 2 with nausea and vomiting, and on one occasion with deafness. Only 2 children complained of tinnitus, while 3 complained of deafness. It was notable that neither tinnitus nor deafness occurred on the 18 occasions when hyperpnoea coincided with a high serum salicylate level. The author concludes that since the incidence of toxic symptoms was so high, treatment with large doses of salicylates should always be carried out in hospital, where adequate supervision is possible.

R. S. Illingworth

1010. **Sequelae of Rheumatic Fever in Men. Four to Eight Year Follow-up Study**

E. P. Engleman, L. E. Hollister, and F. O. Kolb. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 1134–1140, July 24, 1954. 16 refs.

The sequelae of rheumatic fever in adults were studied at the University of California with reference to the medical records and present condition of 135 ex-Service men who had rheumatic fever during the war, the records of a further 80 ex-Service men who had had rheumatic fever but who were not examined being used for comparison. The former group, whose average age was 22 years, were examined clinically and radiologically and questioned about symptoms and physical fitness.

It was found that while many had symptoms of heart disease (precordial pain, dyspnoea, and palpitation) only 32 (23·7%) had definite rheumatic heart disease at the time of the follow-up examination, although 69 were considered to have rheumatic carditis during the initial attack. In none of the patients was there clinical or radiological evidence of arthritis, although 89 complained of pain and stiffness in joints. A few of the patients had to avoid arduous physical work and competitive sports, but 95% were either employed or attending college, the remaining 5% being unemployed because of non-rheumatic disease or psychiatric disorder.

Examination of the records of the 80 control subjects showed that 16 had signs of rheumatic carditis about 3 years after the attack of rheumatic fever, although carditis was present in 35 at the time of the attack. The authors comment on and compare these results with those obtained in similar studies of rheumatic fever in juveniles.

Kathleen M. Lawther

1011. **The Serum Polysaccharide–Protein Ratio (PR) as a Measure of Rheumatoid Arthritis Activity**

R. W. Payne, M. R. Shetlar, J. A. Bullock, D. R. Patrick, A. A. Hellbaum, and W. K. Ishmael. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 775–779, Oct., 1954. 3 figs., 5 refs.

It is known that the serum polysaccharide content is increased and the serum protein levels altered in patients with active rheumatoid arthritis. The serum polysaccharide : protein ratio (P.R.), obtained by dividing the serum polysaccharide concentration by that of the serum protein and multiplying by 100, was calculated in 103 cases of rheumatoid arthritis studied at the University of Oklahoma and Bone and Joint Hospitals, Oklahoma City, and compared with the normal value, which averages 1·76. It was found that increased clinical activity of the disease was accompanied by a corresponding rise in the P.R., and improvement in the clinical state by a fall. There was no significant correlation between the P.R. and the erythrocyte sedimentation rate, but a negative correlation was noted with the serum albumin content, which decreased as the P.R. increased. The ratio is also increased by other inflammatory conditions, cancer, and severe trauma, but the authors suggest that, provided these conditions are kept in mind, it provides a useful objective measure of activity in rheumatoid arthritis.

F. Clifford Rose

1012. **The Agglutination Reaction with Sensitized Erythrocytes as Applied to the Serological Diagnosis of Rheumatoid Arthritis. II. Investigation of the Agglutinating Agent.** (Über die zur serologischen Diagnose der chronischen Polyarthritis angewandte Agglutinationsreaktion mit sensibilisierten Erythrocyten. II. Untersuchungen über das die Agglutination vermittelnde Prinzip)

F. Dickgiesser and F. Harter. *Zeitschrift für die gesamte experimentelle Medizin* [*Z. ges. exp. Med.*] **124**, 501–523, 1954. Bibliography.

Physical Medicine

1013. **Sauna Baths—a Preliminary Report**
N. K. COVALT. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] 33, 216–223, Aug., 1954. 12 refs.

The *sauna* is a hot, dry bath of Finnish origin. Bathers alternate between a very hot room of low humidity and a cool or tepid shower, with a rest in a cool room before repeating the cycle. The author reviews the history and literature of the *sauna* and the many claims made for its health-giving, therapeutic, and hygienic properties. To investigate some of these claims, 5 healthy young females were given a weekly *sauna* bath for 12 weeks. Before and after each bath their weight, temperature, and blood pressure were recorded. No significant changes in weight were noted. In most, but not all, subjects the temperature after the bath was a degree or two above normal, but quickly returned to normal. No significant changes in blood pressure were recorded. All the subjects reported that the baths made them feel " wonderful ".

[This paper cannot be regarded as a serious contribution to scientific knowledge.] *W. Tegner*

1014. **Use of a Recording Dynamometer in Clinical Medicine**
W. RITCHIE RUSSELL. *British Medical Journal* [*Brit. med. J.*] 2, 731–732, Sept. 25, 1954. 14 figs., 1 ref.

The author describes a recording dynamometer in use at the United Oxford Hospitals for measuring the maximum grip. This consists of a system of spring resistances mounted in a frame, with a moving paper strip to record the readings. Both hands may be tested at the same time. The apparatus is useful for the detection of muscle weakness and fatigue in diseases such as myasthenia gravis and myotonia congenita; in focal cerebral lesions; in disorders of motor function such as Huntington's chorea, Wilson's disease, and Parkinson's disease, in which the records obtained are characteristic; or in hysterical or malingering patients.

The apparatus can also be used to estimate the degree of loss of function and for studying the recovery of muscle strength. *J. B. Millard*

1015. **The Management of Low Back Pain**
F. MAY. *Medical Journal of Australia* [*Med. J. Aust.*] 2, 697–701, Oct. 30, 1954. 18 refs.

It is first pointed out that low back pain is such a common complaint among patients seen in hospital departments of physical medicine that the management of these patients warrants consideration. To achieve the best results a full history, with details of the mode of onset of the pain and any subsequent changes, and a careful examination are essential. The spine and lower limbs should be examined to elicit hip movements, areas of tenderness, sensation, reflexes, and Lasègue's sign. Procaine should be injected into tender areas and the examination repeated. When a preliminary diagnosis has been made further investigations should include x-ray examination of the spine, tests for focal sepsis, and estimation of the erythrocyte sedimentation rate, the blood uric acid content, and the haemoglobin level. In females the vagina should be examined to determine whether a lesion of the cervix is present; in males a prostatic smear should be examined microscopically.

Common causes of backache are scoliosis, postural defects causing pelvic tilt, spondylolisthesis, developmental abnormalities, fibrositis, acute infections and toxic conditions due to focal sepsis, cervical or prostatic lesions, disk protrusion and joint lesions, degenerative arthritis, senile osteoporosis, ankylosing spondylitis, fractures, secondary malignant deposits, and osteitis condensans ilii.

In the author's view psychogenic backache is not common. He discusses each lesion and the differential diagnosis, and outlines appropriate treatment, including rest, immobilization, passive or active physiotherapy, and manipulation as indicated. *J. B. Millard*

1016. **The Influence of Electric Stimulation on the Course of Denervation Atrophy**
D. V. SHAFFER, G. K. BRANES, K. G. WAKIM, G. P. SAYRE, and F. H. KRUSEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] 35, 491–499, Aug., 1954. 7 figs., 22 refs.

Although the majority of workers are agreed that the atrophy of denervated muscle can be retarded by electrical stimulation, a more definite understanding of the role of such stimulation and of the most suitable method of its application is needed. Experiments were therefore carried out at the Mayo Foundation on albino rats in which the sciatic nerves had been severed to cause denervation of the muscles. The rats were divided into five groups and treated as follows: (1) in 27 animals one leg only was denervated, stimulation of the denervated muscles with an electronic stimulator being started immediately with the limb stretched and the muscles made to contract against resistance; (2) 27 rats were treated similarly, but without stretching and resistance; (3) in 14 animals stimulation and contraction against resistance was not started until 10 days after denervation; (4) in 21 animals both legs were denervated, stimulation of one being started immediately with contraction against resistance, while the other leg was used as an untreated control; (5) in a control group of 65 rats one leg was denervated and no stimulation was carried out. The muscles studied were the gastrocnemius, soleus, and plantaris. Stimulation was carried out twice daily for 15 minutes at an intensity sufficient to cause vigorous contraction.

It was found that the greatest retardation of atrophy occurred in Groups 1 and 4; if stimulation was post-

poned (Group 3) there was a corresponding decrease in the retardation of atrophy, while stimulation without tension and resistance (Group 2) resulted in a negligible degree of retardation of atrophy. All muscles did not behave similarly, the atrophy being least in the superficial muscles, where the stimulation was most intense. A small series of dogs were treated similarly with similar results.

The authors conclude that denervation atrophy can be delayed by electrical stimulation provided the muscle is stretched and made to contract against resistance, but it is emphasized that in no case can atrophy be delayed indefinitely or prevented entirely. *W. Tegner*

1017. **Principles of Neuromuscular Reeducation**
O. L. HUDDLESTON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1396–1398, Dec. 11, 1954. 1 fig., 8 refs.

1018. **Experimental Iontophoresis: Studies with Radioisotopes**
E. P. O'MALLEY, Y. T. OESTER, and E. G. WARNICK. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **35**, 500–507, Aug., 1954. 5 figs., 11 refs.

The aim of the experiments here reported from Loyola University, Chicago, was to investigate the extent and distribution of certain radioactive isotopes introduced into rats by ionization. The rats were anaesthetized and the ions introduced by means of electrodes applied to the left fore leg and the middle of the tail. The radioactive materials used were phosphorus (^{32}P) as sodium phosphate, iodine (^{131}I) in sodium bisulphite solution and as sodium diiodofluorescein, and sodium (^{24}Na) and calcium (^{45}Ca) as the chlorides. Three types of experiment were carried out: (1) the isotopes were applied under the electrode of the same charge and were therefore driven into the animal; (2) the isotopes were applied under the opposite electrode; and (3) the isotopes were placed in position, but no current was applied.

In the last two types of experiment only minute amounts of the radioactive substances were found in the tissues on analysis. In the first series of experiments, however, the isotopes were found to have been introduced into the body, though their distribution in the tissues suggested that this occurred not along the tissue planes, but by the systemic circulation in the same way as isotopes introduced by other routes. The possibility that the introduction of the ions had been affected by the change of temperature induced by the passage of current was ruled out by the fact that a reversal of the current, although producing similar temperature effects, resulted in no appreciable introduction of ions. *W. Tegner*

1019. **Recent Advances in the Technique of Progressive Resistance Exercise**
I. J. MACQUEEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1193–1198, Nov. 20, 1954. 7 figs., 15 refs.

Writing from the Department of Anatomy, Sheffield University, the author discusses what we may learn about the technique of progressive-resistance muscular exercises from weight-lifters and athletes who, it is pointed out, use simple weights as resistance, rather than springs or complicated apparatus. There are two distinct aims and programmes of these exercises: one to promote muscle hypertrophy and bulk, and the other to increase muscle power. The former programme will also increase muscle power, but not to the same extent as the " power programme ".

The essential feature of the " muscle-hypertrophy programme " is the repetitive lifting of a maximum weight by various muscle groups. There are several refinements in this technique as follows. (1) " Flushing ", which consists in changing the position of the body in lifting the weight, but using the same muscles; this is believed to keep the muscles well flushed with blood. (2) " Muscle cramping ", in which more than the maximum load is added to the already contracted muscle, and the muscle is exercised over a very limited range; this exercise can be tolerated for only a few minutes at a time, and is often followed by a mottling of the skin like the flare of the " triple response "; after cramping, the muscle must be fully stretched to prevent " muscle binding ". (3) The carrying out of the exercise in front of a mirror; this helps to increase cortical awareness of the muscles which are being exercised. (4) The " peak contraction " principle, whereby it is ensured that resistance is maximal at the peak of contraction. (5) " Cheating ", in which other muscles are brought into use to assist the muscle which is being particularly exercised; it has been found that this recruitment does in fact develop the intended muscle, though the reason for this is not clear.

The power programme consists essentially in decreasing the number of repetitions of weight lifting while correspondingly increasing the resistance (usually 10 to 20 lb. (4·5 to 9 kg.)) at each attempt. After the maximum possible weight has been lifted once, weights beyond the power of the individual by about 5 lb. (2·3 kg.) are attempted and persisted with until a new maximum is established. A refinement of the power programme is the " washer " or " miniature disk " technique, whereby after a maximum lift only a small addition ($\frac{1}{2}$ lb. (220 g.)) is added to the weight, and this is lifted by " cheating ", it being hoped that later this weight can be lifted by the " strict " method.

Two new methods of training now being tried out are briefly mentioned. In one either a great number of repetitions of weight lifting is made possible by gradually decreasing the weight or, conversely, the weight is gradually increased until the lifter fails; in the other an exercise involving lifting a maximum weight 10 times in succession is carried out once or twice every hour throughout the day for 6 days a week. The author suggests in conclusion that the techniques described, which have been worked out empirically by laymen, must have important clinical applications and implications for all those concerned with physical medicine.

W. Tegner

1020. **The Orthopedic Treatment of Chronic Arthritis**
J. G. KUHNS. *Missouri Medicine* [*Missouri Med.*] **51**, 1002–1003, Dec., 1954.

Neurology and Neurosurgery

1021. **Ulceration and Malacia of the Upper Alimentary Tract in Neurologic Disorders**
J. MacD. Watson and M. G. Netsky. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **72**, 426–439, Oct., 1954. 3 figs., 30 refs.

From a review of the literature concerning the possible neurogenic origin of peptic ulcer the authors conclude that it has been established (1) that there is an anatomical pathway between the hypothalamus and the gastrointestinal tract; (2) that there is evidence that hypothalamic activity may result in peptic ulceration, either from excessive sympathetic activity producing " visceral circulatory stasis " or from shock; and (3) that there is reason to believe that cortical or subcortical centres may also be concerned in the production of gastrointestinal pathological changes through their influence on the hypothalamic or vagal centres.

An association between the central nervous system and the alimentary tract is also suggested by the occurrence of gastrointestinal disorders in certain chronic neurological diseases. In 6 cases reported here the primary conditions included disseminated sclerosis, asphyxia, cerebral infarction, and metastatic melanoma, and in each case necropsy revealed gastrointestinal malacia or ulceration (proved to have been present ante mortem). In addition, a further 38 cases of associated neurological and gastrointestinal disease have been collected from the literature and are analysed in detail. It is postulated that cortical or " supra-diencephalic " centres have a moderating influence upon the diencephalic and vagal centres, and that failure of this control may result in ulceration or malacia of the upper alimentary tract. *Adrian V. Adams*

1022. **Clinical Evaluation of Focal Depression of Voltage in Electroencephalography**
W. J. Friedlander. *Neurology* [*Neurology*] **4**, 752–761, Oct., 1954. 6 figs., 45 refs.

Focal depression of voltage in the electroencephalogram (EEG) is known to occur in many pathological conditions. The study here reported from the Veterans Administration Hospital, San Francisco, represents a careful attempt to answer the vexed question whether this local depression of amplitude has any useful clinical significance; the author gives due recognition [notably absent from some papers] to the difficulties of correctly assessing the type and amount of depression in the record.

In the examination of 1,010 EEG recordings from 774 patients, minimal focal depression was found in those of 168 patients (22%), and moderate or marked depression in 93 (12%); included in the latter were the EEGs of 40 patients (5·2% of the total) which showed also local alteration of rhythm, and it was only in this group that fair correlation was found between the EEG appearances and clinical evidence of a local pathological condition. *W. A. Cobb*

BRAIN AND MENINGES

1023. **Puerperal Hemiplegia**
H. Stevens. *Neurology* [*Neurology*] **4**, 723–738, Oct., 1954. 5 figs., 47 refs.

The author reports, from George Washington University Hospital, Washington, D.C., 8 cases of cerebral venous thrombosis occurring during the puerperium, in 6 instances within 24 hours of delivery and in the other 2 on the 12th and 17th days respectively. Associated symptoms included severe headache, repeated focal seizures, and transient signs of bilateral cerebral involvement. A notable feature observed in 4 of the cases, and apparently not previously emphasized, was the finding of a widely fluctuating hypertension. All the patients made a good recovery both from the neurological defect and the hypertension.

In discussing these cases, the author comments that the diagnosis is not difficult, but the condition is not widely known and too often is misdiagnosed as postpartum eclampsia. With regard to treatment, anticoagulants are felt to be too risky. As the rise in blood pressure may well be reflexly determined by an increase in cerebral vascular resistance it therefore should not be lowered by drugs. Anticonvulsants are, however, certainly needed and measures to reduce intracranial pressure may also be required.

[The author gives full credit to previous work on this subject in Europe, and especially in Britain, where the condition is probably better known than in the United States.] *N. S. Alcock*

1024. **Diamox: a Carbonic Anhydrase Inhibitor. Its Use in Epilepsy**
S. Merlis. *Neurology* [*Neurology*] **4**, 863–868, Nov., 1954. 12 refs.

" Diamox " is a sulphonamide derivative with the chemical designation 2-acetylamino-1 : 3 : 4-thiadiazole-5-sulphonamide, but its organic structure and pharmacological activity are totally different from the sulphonamides used as bacteriostatic agents. It is a potent inhibitor of carbonic anhydrase, an enzyme which plays an important role in carbohydrate metabolism of the central nervous system and may also conceivably play a part in increasing the speed of propagation of nerve impulses. The literature on the physiological action of the enzyme is briefly reviewed.

The author then records the results obtained with diamox in 47 cases of chronic epilepsy with psychosis treated at the Central Islip State Hospital, New York, in 35 of which previous medication had proved ineffective. The dose of diamox ranged from 500 to 1,000 mg. daily. In only 13 cases was diamox alone sufficient to control the epileptic seizures, other additional drugs being required to gain adequate control. The drug proved to be of value in 35 out of 47 patients, suppression of 40

to 80% of the fits being achieved in 6 cases, and of 80 to 100% in 29 cases; 12 patients were not benefited, but none was considered to be worse. No serious toxic effects were noted, although 4 patients experienced transient episodes of flushing, headaches, and feelings of fatigue; gastrointestinal upsets appeared early in the course of treatment, but were readily controlled by the administration of alkalis and milk. It is interesting to note that those patients who showed a marked alteration in the electroencephalogram following hyperventilation were most likely to benefit from diamox. Of the 29 patients showing most improvement, 3 were well enough to be discharged and have remained free of fits for periods up to 8 months. *N. S. Alcock*

1025. **Migraine and Epilepsy.** (Migräne und Epilepsie) W. BÄRTSCHI-ROCHAIX. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **84**, 1139–1144, Oct. 2, 1954. 4 figs., bibliography.

Discussing the possible relationship between migraine and epilepsy the author, who is head of the Electroencephalographic Department of the Medical Clinic of the University of Berne, points out that migraine is 10 to 20 times commoner than epilepsy, and that the frequency with which the two occur together in the same individual is not too great to be attributable to chance. In view of the clinical differences between the two diseases and the entirely dissimilar changes found in the electroencephalogram the author prefers to regard them as two separate entities, although they each represent an abnormal outburst of activity in one of the constituents of the nervous system—namely, the neuronal and vasomotor systems—in response to physical, chemical, biological, toxic, or psychological stimuli which may be identical. The response in each case follows a fixed pattern on each occasion, the symptoms of migraine being derived largely from abnormal changes of calibre in the intracranial or extracranial vessels, whereas those of epilepsy are determined by the site of origin and route of spread of the discharge in the neuronal system of the brain.

[This is a well-reasoned article.] *G. S. Crockett*

1026. **Photogenic Epilepsy: Self-precipitated Attacks**
E. G. ROBERTSON. *Brain* [*Brain*] 77, 232–251, June, 1954. (Received Sept., 1954.) 6 figs., 20 refs.

A detailed account is given of 7 cases of photogenic epilepsy seen within a period of 12 months at the Royal Melbourne and Royal Children's Hospitals, Melbourne, in which attacks could be precipitated voluntarily by the subject by rhythmical interruption of sunlight falling on the eyes, either by movement of the fingers or hand in front of the face or by blinking. The attacks were usually slight (" absences " or petit mal) and of brief duration, with varying degrees of impairment of consciousness. If the process was repeated over a long period jactitation and a major attack might occur, and in a few patients major attacks occurred independently. Electroencephalography during a self-induced attack showed varying forms of spike and slow wave discharges of high voltage, usually irregular and of brief duration. The dysrhythmia lessened and disappeared when the intensity of illumination was reduced.

Encouragement of the patient to avoid making the provoking movement proved to be the best method of treatment. There was little response to the drugs of the dione group, in spite of the presence in some patients of 3-per-second slow wave and spike discharges.

J. MacD. Holmes

1027. **A Study of the Effectiveness of Drug Therapy in Parkinsonism**
H. A. KAPLAN, S. MACHOVER, and A. RABINER. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 398–411, May, 1954. 1 fig.

A comparison of the efficacy of a placebo, benzhexol hydrochloride (" artane "), " panparnit ", and hyoscine in the treatment of 35 patients suffering from Parkinsonism is reported in this paper from the State University of New York. The subjective effect observed by the patients, the results of a neurological examination, and certain more objective findings obtained by means of the electromyograph, 5 different tests on the Purdue pegboard, and the dynamometer were used for assessing the results. Each patient served as his own control and received in turn each of the 3 drugs and a placebo for a period of 4 weeks.

The subjective improvement noted by the patients during drug therapy was distinctly superior to that noted during the period of administration of the placebo. The electromyographic tracings taken before and during treatment showed that although the drugs did not lessen the tremor, this increased during treatment with the placebo. The authors suggest that this difference was due to the fact that in most cases the placebo was given after the patient had become adjusted to one of the drugs, the increase in tremor beyond the original base level being the result of withdrawal of the drug.

Four of the 5 pegboard tests showed a statistically significant improvement after administration both of the drugs and the placebo. Treatment did not improve performance with the dynamometer. The authors conclude that except for a definite subjective improvement with the drugs there was no significant difference between these and the placebo in their effect on symptoms.

Richard de Alarcón

1028. **Treatment of Parkinsonism with Pagitane Hydrochloride. Results in 142 Patients**
A. ZIER and L. J. DOSHAY. *Neurology* [*Neurology*] 4, 682–689, Sept., 1954. 8 refs.

The authors report, from the Presbyterian Hospital (Columbia University), New York, the results of a clinical trial of a new synthetic drug, "pagitane" hydrochloride (1-phenyl-1-*cyclo*pentyl-3-piperidino-1-propanol hydrochloride, a substance related to " artane ") in 142 cases of Parkinsonism. The series included 45 cases of the postencephalitic type, 50 of the idiopathic type, and 47 of arteriosclerotic type, and all were selected in that they had failed to respond to treatment with other drugs. The maximum period of treatment was 15 months, and no patient was classified as improved unless he had been

treated for a minimum of 8 weeks. The daily maintenance dose ranged from 7·5 to 15 mg.; only 28% of the patients received pagitane alone, the rest requiring additional drugs at some time during the test but in most cases only for very short periods, so that on the whole it could be said that pagitane was the principle drug employed. Evaluation was based on frequent clinical observation and on reports from the patients and their relatives.

The over-all results showed that 66% were improved, 28% remained unchanged, and 6% became worse. Pagitane acted principally on the rigidity, sialorrhoea, and mild forms of tremor, and also as a cerebral stimulant. For cases with major tremor and advanced rigidity other drugs had to be added. In 9 out of 18 cases pagitane proved very effective in the control of oculogyric crises, which could be aborted by taking 5 to 10 mg. just before the onset of the crisis. The drug, contrary to earlier reported observations, was found to maintain its effectiveness for over a year. Its beneficial action was very noticeable in cases in which artane was losing its effect. Pagitane appeared to cause no mental clouding, its main side-effects being dryness of the mouth (22% of cases) and blurred vision (13%). Pagitane was also tried, but without success, in 2 cases of familial tremor. In one case of Huntington's chorea, however, it reduced the involuntary movements considerably, and improvement was also observed in a case of dystonia musculorum deformans. *Richard de Alarcón*

1029. **Pseudotumor Cerebri**
G. D. Zuidema and S. J. Cohen. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 433–441, Sept., 1954. 11 refs.

A certain proportion of cases of increased intracranial pressure do not reveal any abnormality on examination by ventriculography or arteriography; such cases are characterized by (1) increased intracranial pressure, (2) a normal ventricular system, and (3) a cerebrospinal fluid which is normal except for the increased pressure. This syndrome has been known variously as pseudotumor cerebri, intracranial hypertension of unknown aetiology, serous meningitis, or otitic hydrocephalus. There is little doubt that a number of different pathological entities are concerned in the aetiology, of which perhaps dural sinus thrombosis is one of the most important.

In order to throw further light on this problem the authors decided to follow up as many as possible of 80 such cases treated at Johns Hopkins Hospital between 1937 and 1953, of which 22 were reported by Dandy in 1937 (*Ann. Surg.*, 1937, **106**, 492). Twelve of these patients were traced, and 10 were found to be living and well, the other 2 having died—one following surgical treatment for an intracranial aneurysm and one probably of disseminated sclerosis. This experience suggests a fairly good long-term prognosis. Of Dandy's 22 patients, 16 were female.

Of the other 58 cases, further study of the records showed that 11 were probably cases of dural sinus thrombosis, 4 were later found to have brain tumour, 3 died after unfruitful craniotomy and no necropsy was permitted, and one was complicated by rheumatic carditis with mitral stenosis, thus leaving 39 cases of classic pseudotumor cerebri; these are analysed. The sex incidence (29 females and 10 males) showed female predominance of 3 to 1, while the highest age incidence was in the age group 20 to 30 years. Different methods of treatment, including repeated lumbar puncture, are discussed, and the indications for subtemporal decompression in this condition are presented.

It is emphasized that the diagnosis of pseudotumor cerebri is one of exclusion, only to be made after exhaustive diagnostic procedures have been carried out. The authors feel, however, " that many, or perhaps even most, of the cases now designated as pseudotumor cerebri are in reality caused by unrecognized dural sinus thrombosis ". *J. V. Crawford*

1030. **Acute Head Injuries in Boxers. Clinical and Electroencephalographic Studies.** [In English]
L. E. Larsson, K. A. Melin, G. Nordström öhrberg, B. P. Silfverskiöld, and K. Öhrberg. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] Suppl. 95, 1–42, 1954. 7 figs., bibliography.

CRANIAL NERVES

1031. **Results of Decompression Operation for Trigeminal Neuralgia**
J. G. Love and H. J. Svien. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 499–504, Sept., 1954. 1 fig., 3 refs.

In 1952 Taarnhøj (*J. Neurosurg.*, **9**, 288) introduced the operation of intradural decompression of the Gasserian ganglion and the posterior root of the 5th nerve for the relief of trigeminal neuralgia. The present authors use an extradural approach and in this paper report their results in 100 cases so treated at the Mayo Clinic between June, 1952, and March, 1954.

The results were as follows. One patient died of coronary disease 9 days after operation; in one case a transient oculomotor palsy developed, which cleared in a month; there were no cases of palsy of the 4th nerve; 16 patients suffered from postoperative facial palsy (9 very slight), this high incidence being attributed to the more extensive reflection of the dura mater required; herpes occurred in 25 cases postoperatively, and subjective sensory impairment, consisting in paraesthesiae and dysaesthesia, was noted in 13 patients, but usually cleared in a few weeks. Sensory loss occurred in 14 cases, but in only one was it profound. No case of keratitis was observed. Relief of pain was immediate and complete in 51 patients, the remaining 49 having continuance of pain in varying degree. In 4 it was so severe that further procedures (posterior-root section or alcohol block) were required; in the other 45 cases it was much less severe.

The maximum follow-up period has been 22 months and the over-all figures show that of the 100 patients, 58 experienced relief, 31 had recurrence of pain, and in 11 cases the results were indeterminate. Analysis of the figures showed that in half the failures pain recurred within the first month; in only 3 cases did pain recur

after one year of relief. The authors agree that the relief of pain by this procedure is less than when the posterior root is sectioned, but suggest that preservation of sensation in the face, eye, and tongue may be worth the risk of failing to obtain relief of pain by this non-mutilating procedure. *J. V. Crawford*

1032. **Atypical Facial Pain**
A. M. G. CAMPBELL and J. K. LLOYD. *Lancet* [*Lancet*] 2, 1034–1038, Nov. 20, 1954. 3 figs., 16 refs.

The clinical symptoms in 40 cases of atypical facial pain are described in this paper from Bristol Royal Hospital. The presenting symptom in all the cases was pain in the face, neck, and head, which was described as burning or boring and was widely distributed beyond the limits of any one nerve division. It was usually unilateral and could easily be distinguished from the pain of both migraine and trigeminal neuralgia. In 22 cases the pain was constant, while in the remainder it was intermittent, the acute attack lasting several hours to 3 days. In many cases unilateral flushing, sweating, lacrimation, pupillary changes, or Horner's syndrome accompanied the pain. There was no constant precipitating factor, but in 16 cases the pain could be exacerbated by flexion and relieved by extension of the neck. The relationship of the pain to disturbance of sympathetic pathways with the liberation of histamine and to cervical spondylosis is discussed.

Immobilization of the neck in slight extension for 4 to 8 weeks by means of a plaster collar gave complete or almost complete relief in 18 out of 25 cases; in some cases a permanent plastic collar was supplied. Cervical sympathectomy was carried out in one case with complete relief of pain. As blocking of the great auricular nerve with procaine gave temporary relief in one case, this nerve was sectioned in 17 cases, the results being "good" in 9 and "moderate" in 3. In 6 of these, however, there was a relapse within one to 5 weeks; in the remaining 6 no relapse occurred during a follow-up period of 4 weeks to 6 months. *L. G. Kiloh*

NEUROMUSCULAR DISEASES

1033. **Investigations of Muscular Weakness in Middle Life: the So-called Menopausal Muscular Dystrophy**
M. BONNIN and W. R. ADEY. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] 3, 171–181, Aug., 1954. 12 figs., 17 refs.

The type of myopathy which occurs predominantly in women at or after the menopause and hence has been called menopausal muscular dystrophy does not seem to have been recognized before 1936, when 2 cases were described by Nevin (*Quart. J. Med.*, 1936, **5**, 51). The present authors report 5 cases seen at the Royal Adelaide Hospital in which the main symptom was muscular weakness, without wasting, confined to the proximal muscles of the limbs. The diagnosis of myopathy was confirmed by histopathological studies and also by electromyography (EMG), although the findings in the latter are not specific to this condition only, but would be consistent with a diagnosis of dystrophy or chronic polymyositis. Indeed, the authors describe a 6th patient who was suffering from acute polymyositis and in whom the EMG changes were similar. There seemed to be some evidence, both clinical and electrical, that the cases of myopathy showed some improvement after the administration of mixed tocopherols. There was less clear evidence that cortisone had any therapeutic value. The series included one male patient, a man aged 62. The aetiology of the disease, which is obscure, is discussed; in none of the present cases was there a family history of any muscular disorder. *Hugh Garland*

1034. **On the Classification, Natural History and Treatment of the Myopathies**
J. N. WALTON and F. J. NATTRASS. *Brain* [*Brain*] 77, 169–231, June, 1954. (Received Sept., 1954.) 15 figs., bibliography.

A clinical survey of 105 cases of myopathy is presented, with particular reference to the classification and natural history of this group of disorders. The authors' analysis of clinical and genetic data leads them to the conclusion that the more commonly occurring cases of muscular dystrophy should be classified into three broad groups, the Duchenne, facioscapulohumeral, and limb-girdle types. Other forms of myopathy which are clinically and genetically distinctive and occur less frequently include the distal, ocular, congenital, and local forms, as well as certain myopathies of endocrine and metabolic origin and others which appear to be related in some way to the collagen diseases.

From observations upon cases of myotonia with and without dystrophy they conclude that a single disease process, which they call the "myotonic syndrome", is common to all, dystrophia myotonica, myotonia congenita, and paramyotonia representing different modes of presentation.

Under this classification the series of 105 cases was made up of 48 cases of the Duchenne, 15 of the facioscapulohumeral, and 18 of the limb-girdle type, 2 cases of the distal and one of the ocular form, and 21 cases of the "myotonic syndrome" (15 of dystrophia myotonica and 6 of myotonia congenita). The clinical features of each type are analysed and tabulated in full detail. The electrocardiogram was abnormal in 12 of the more advanced cases of the Duchenne type, while more severe abnormalities were present in tracings from 11 of the cases of dystrophia myotonica. The urine in 89 cases was examined for the presence of ribose, the result being positive in 12 cases and negative in the remainder; but since specimens from 2 patients with motor neurone disease also gave a positive reaction, the test is clearly of no value in diagnosis.

The results of a carefully controlled therapeutic trial involving a total of 98 cases are reported. The remedies used were α-tocopherol, wheat-germ oil, mixed natural tocopherols, nicotinamide, and a control substance. In no case was objective evidence of improvement obtained, and statistical evaluation of the results indicated that none of the remedies had a significant effect on the course of the disease. *J. MacD. Holmes*

Psychiatry

1035. The Use of an Alkaloid of Rauwolfia in Neuropsychiatry. (Impiego di un alcaloide della rauwolfia in neuropsichiatria)

S. COLOMBATI and P. BENASSI. *Gazzetta medica italiana* [*Gazz. med. ital.*] **113**, 301–303, Oct., 1954. 8 refs.

At the Clinic for Nervous and Mental Diseases of the University of Bologna 25 psychiatric and neurological patients, 5 suffering from mania, 5 from neurasthenia, 4 from depression, 3 from hysteria, 3 from post-encephalitic Parkinsonism, 2 from obsessional states, 2 from paraphrenia, and one from Huntington's chorea, were treated with "serpasil" (reserpine), in doses of 0·3 to 3 mg. daily. As a result the manic patients became tranquil, the neurasthenic patients showed lessened irritability, those with depression became free from anxiety, the hysterics lost much of their suggestibility, the patients with obsessional states experienced a diminished intensity in their thoughts, while the paraphrenics showed symptomatic improvement, one of them reporting freedom from auditory hallucinations. There was no change in the tremors of postencephalitic Parkinsonism, but a diminution in the movements was noted in the case of Huntington's chorea. Apart from some reduction in the blood pressure and slowing of the pulse rate, the only side-effects observed consisted in diarrhoea (5 cases) and an urticarial rash (one case) which responded readily to the usual remedies. *P. Cassar*

1036. Experimental Observations on "Psychosomatic" Mechanisms. 1. Gastrointestinal Disturbances

J. D. FRENCH, R. W. PORTER, E. B. CAVANAUGH, and R. L. LONGMIRE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 267–281, Sept., 1954. 6 figs., 24 refs.

At the University of California School of Medicine, Los Angeles, experiments were carried out on 17 healthy monkeys to study the changes induced in the gastrointestinal tract by stimulation of the central nervous system. Electrical stimulation was applied to the hypothalamus or to other areas of the brain stem for control purposes for periods up to 74 days. All the animals were later killed and necropsy performed. Gross lesions were found in the upper gastrointestinal tract in 6 of the 10 test animals; no such lesions were found in the 7 control animals. In 4 the lesions were in the prepyloric or post-pyloric region, while in 2 they spread throughout the stomach. Prolonged stimulation in or near the hypothalamus was the causal factor in all these cases. It was not possible to identify one particular area as exercising a special influence upon the stomach. The lesions produced strongly resembled peptic ulcer.

[This is a rather laboured experimental demonstration of what we already know—namely, that gastrointestinal function and structure are influenced by impulses from the central nervous system. It underlines the conclusion that impulses relayed in the hypothalamus can produce lesions similar to, and perhaps identical with, peptic ulcer.] *Desmond O'Neill*

1037. The Experimental Administration of *Celastrus paniculata* in Mental Deficiency Practice

J. V. MORRIS, R. C. MACGILLIVRAY, and C. M. MATHIESON. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **59**, 235–244, Oct., 1954. 15 refs.

Celastrus paniculata appears to be of little value in the treatment of oligophrenia. It is possible that the euphoria produced by its administration may be responsible for its traditional reputation as a stimulant of intelligence and memory. Further investigations of the mood changes are needed to determine whether they are permanent or transitory.

The drug may be of use in psychological investigations, but the variability of the mood changes suggests that it would be of little benefit in the treatment of depressive states.—[Authors' summary.]

1038. Pulmonary Tuberculosis Mortality in a Mental Deficiency Hospital

B. W. RICHARDS. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **59**, 245–253, Oct., 1954. 9 refs.

The investigation described in this paper was undertaken to provide statistical information concerning mortality from pulmonary tuberculosis in a hospital for mental defectives, the period covered being 1941–51, during which time the number of inmates rose from about 1,300 to 1,500. The patients were of both sexes and of all ages. So far as possible, patients with low-grade mental deficiency were segregated from those with high-grade mental deficiency, but the accommodation and space available for the two groups were similar.

The annual mortality from tuberculosis per 1,000 patients was much higher than the rate in the general population, a finding confirmed by other workers. Analysis of the figures by sex and grade of mental defect showed that the absolute mortality from pulmonary tuberculosis was higher in males than in females, and higher in low-grade than in high-grade mental defectives. It also revealed that the sex difference was almost entirely accounted for by the mortality in low-grade defectives, there being no appreciable sex difference in the mortality among patients suffering from high-grade mental deficiency. The number of deaths from causes other than tuberculosis was also higher among low-grade mental defectives, but in this group was higher in females than in males.

Mongols accounted for almost one-third of the patients with pulmonary tuberculosis, in spite of the fact that the number of mongols in the hospital was only about one-fifteenth of the total and about one-seventh of the number of low-grade defectives, and the death rate

among them was much higher than among "other low grades". As regards duration of life after tuberculosis was diagnosed, 75% of mongols died within 6 months, whereas 75% of the others lived for up to one year.

It is pointed out that diagnosis is more difficult among defectives than among the general population and among low-grade than among high-grade defectives. Many deaths from tuberculosis occur within 6 months of the patient's admission, suggesting that *x*-ray examination of the chest should be carried out in all cases on admission.

It is considered that the high mortality from all causes among low-grade defectives may be explained by physical disability, lack of mobility, and poor respiratory movements or inability to cough "for physical or mental reasons". No satisfactory explanation was found for the excessive susceptibility of male low-grade mental defectives, but it is suggested that a sex-linked condition may be associated with low resistance to the disease, as mongolism apparently is. *E. M. Watkins*

1039. **Mental Disturbances in Thromboangiitis Obliterans.** (Психические нарушения при облитерирующем тромбангиите)
A. N. Popova and L. P. Demidova. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 819–828, Oct., 1954. 9 refs.

After reviewing the general features of thromboangiitis obliterans and its neurological and psychiatric manifestations, the authors, writing from the Psychiatric Department of the Moscow Postgraduate Medical School, report in detail 3 cases of this condition, all of which were dominated by a psychotic syndrome. It was possible to trace the intermittent course of the disease through the following three phases: (1) an asthenic phase, (2) a period of marked mental disturbance, and (3) a phase of increasing dementia. Some improvement in the mental condition followed treatment with vasodilator and anticoagulant substances. *L. Crome*

TREATMENT

1040. **Prognosis of Depression with Electrical Treatment**
D. L. C. Thomas. *British Medical Journal* [*Brit. med. J.*] 2, 950–954, Oct. 23, 1954. 3 refs.

The author studied the effects of electrical treatment on 307 patients with depression admitted to St. George's Hospital, London. Among them were 240 with endogenous, 50 with involutional, and 17 with reactive depression. There were also 12 cases showing paranoid or schizophrenic features, but these are not reported in detail.

From the records details were obtained of the number of electrical treatments given and their spacing, clinical response, and the length of stay in hospital. An attempt was made to find: (*a*) any differences between diagnostic groups in their response to treatment; (*b*) any indications of the minimum length of time a patient should be kept in hospital to guard against relapse; and (*c*) the chances of recurrence after recovery or improvement. "Relapse" is used to indicate that the patient had needed further treatment within 4 weeks of the initial course; and "recurrence" to describe any deterioration occurring more than 4 weeks after the initial course but within the following 12 months.

Of these patients, 213 (69%) recovered or were "much improved," 85 (28%) were "improved," and 9 (3%) unchanged. Cases of reactive depression did least well; and cases of endogenous depression with hysterical or obsessional symptoms did less well than those of other forms of depression. Patients who did not suffer relapse remained in hospital between 5 and 6 weeks and received an average of 5·4 treatments, except those with involutional depression, who stayed 7 weeks and had an average of 6 treatments.

Relapse during treatment occurred in 81 (26% of all cases), in 98% of them between 8 and 16 days after the end of the initial course. The involutional group had the largest proportion of relapses—23 out of 50 (46%). Patients who relapsed needed an average of 2·4 additional treatments.

Of the 219 cases in which a 12-month follow-up was possible, 50 (23%) showed recurrence, the rate being highest among cases of involutional and agitated depression and of depression with hypochondriasis. Recurrence bore no relation to the degree of recovery after treatment, but a close relation to the relapse rate during treatment. Of the 59 cases which relapsed, 24 (41%) showed recurrence within 13 months, as opposed to 26 (16%) of the 160 which did not relapse.

Of the 12 patients with paranoid and schizophrenic features, 11 recovered or were much improved and only one recurred. The author suggests that, although the number of these cases was small, the results indicate that the prognosis of depression with schizophrenic features is similar to that of other forms of depression.

E. M. Watkins

1041. **West Virginia Lobotomy Project**
W. Freeman, H. W. Davis, I. C. East, H. S. Tait, S. O. Johnson, and W. B. Rogers. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 939–943, Nov. 6, 1954. 3 figs.

During the year 1952, 228 patients in West Virginia State mental hospitals were subjected to transorbital lobotomy. One year later 85 (37%) were out of hospital; 4 patients died from the operation. Of a control group of 202 patients whose relatives had refused permission for operation, only 5 were well enough to be discharged, 2 had died, and 8 were improved. Most of the patients treated were chronic cases, only 32 had been in hospital for less than one year, and 93 had been in-patients for over 5 years; schizophrenics accounted for 173 of the total series. After operation, the proportion of disturbed cases fell from 64% to 21%, and that of patients able to undertake some kind of work rose from 4% to 8%.

During 1953, 285 operations were performed, 17 being second operations; by May, 1954, 107 patients (38%) had been discharged. Between January and March, 1954, 115 patients were operated on (9 for a second time), and at the end of May, 1954, 44 (38%) were out of

hospital. Thus in a total of 628 lobectomies performed on 602 patients, postoperative deaths numbered only 10, and some 38% of the patients were enabled to return to their homes. The importance of explanation to the patient's family is stressed. Meetings of relatives were held at which the operation was described and the ways in which the family could help in caring for the patient were outlined, the three stages through which the patient would probably pass being described. The first stage, lasting about 2 weeks, consists of a period of friendliness, indolence, confusion, and forgetfulness; the second, lasting from 6 weeks to 6 months, is characterized by instability, defiance, and perhaps resurgence of complaints; the third stage is a period of adjustment. During the second stage, the relatives were asked to bring the patients back for further treatment if the task of looking after them became too difficult. In some cases a second operation may be successful after initial failure; rehabilitation by other methods of treatment is more effective after than before lobotomy. Details of the operative procedure and postoperative management are given, and the economic benefits to be expected are discussed. *G. de M. Rudolf*

1042. **Prefrontal Ultrasonic Irradiation—a Substitute for Lobotomy**

P. A. LINDSTROM. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **72**, 399–425, Oct., 1954. 11 figs., bibliography.

Experiments performed at the University of Pittsburgh on the rabbit showed that transcranial irradiation of the brain with high-frequency sound vibrations resulted in a very variable degree of injury which was concentrated at the meninges and surface of the cortex, the effects of ultrasonic vibration tending to be greatest at an interface between media of different densities. By direct irradiation of the exposed brain, however, lesions of controllable intensity, ranging from a reversible or minimal effect to gross necrosis and extending deep into the white matter, could be produced with minimal damage to the cortex and with little ill effect on the animal as a whole. Allowing for the greater size of the human brain, it seemed reasonable to expect that a similarly controlled effect could be obtained in man, and that localized destruction of tissue could be produced in the frontal lobe by this means without the hazards and complications associated with surgical lobotomy.

A clinical trial was therefore carried out at the Veterans Administration Hospital, Pittsburgh, on 20 patients, 16 of whom had intractable pain from malignant metastatic disease combined, in some cases, with anxiety, depression, and narcotic addiction, one had leukaemia with intolerable pain from neuralgia of the brachial plexus and *x*-ray reaction, one had amyotrophic lateral sclerosis with episodes of profound depression, one had advanced Parkinsonism with narcotic addiction, and the last was an uncontrollable epileptic with very severe behaviour disorder. The sound head was introduced through bilateral trephine holes 1¼ to 1½ inch (3·2 to 3·8 cm.) in diameter over the frontal areas, with Ringer's solution, continuously flowing in order to prevent local trauma from heat, as a coupling agent. The beam was directed at the anterior tip of the lateral ventricle and a frequency of 1,000 kilocycles per second was used at an average intensity of 7 watts per sq. cm., the exposure time varying from 4 to 14 minutes over each lobe. No postoperative complications, noticeable personality changes, inertia, stupor, or incontinence resulted from the treatment, and there was no impairment of insight or judgment. Electroencephalography was carried out before and after treatment in half the cases, and revealed no abnormality. Ten patients suffering from excruciating pain experienced almost complete relief for periods ranging from 2 weeks to 12 months after the treatment. Four others with intractable pain continued to have intermittent bouts of moderate pain, but they were less anxious and the pain appeared to be more readily controlled by analgesics. Examination of the brain at necropsy on 15 patients who died from malignant disease provided no evidence that the treatment had been a contributory cause of death. The lesions found were wholly confined to areas traversed by the ultrasonic beam, the most typical changes being slight gliosis in the white matter, with disfigurement and disruption of myelin sheaths. In the cortical areas traversed there were degenerative changes or actual loss of ganglion cells when high-energy radiation had been used, but the general architecture was undisturbed. Emigration of a few erythrocytes could be seen in places, but damage to the vessel walls was minimal. *Adrian V. Adams*

1043. **Reserpine (Serpasil) in the Management of the Mentally Ill and Mentally Retarded. Preliminary Report**

R. H. NOCE, D. B. WILLIAMS, and W. RAPAPORT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 821–824, Oct. 30, 1954. 1 ref.

Reserpine (" serpasil ") was administered for periods ranging up to 7 months to 74 violently disturbed psychotic patients at the Modesto State Hospital, California. All the patients had been ill for a long time and had proved refractory to other methods of treatment. Treatment was initiated with intravenous injections of 1 to 10 mg. of reserpine given daily or every other day for the first week, together with 0·5 mg. by mouth 4 times a day. No alarming reactions occurred. The side-effects noted were flushing of the face and extremities, shivering, mild vertigo and weakness, and lowering of the blood pressure and pulse rate. As a result of this treatment the patients became tranquil, sociable, and amenable to psychotherapy and rehabilitation, so that seclusion and restraint were almost eliminated. Remissions occurred in 20 cases and 8 patients could be discharged. The authors consider it too early to state whether reserpine therapy must be continued indefinitely.

A group of 15 mental defectives whose I.Q. varied from 2 to 34 and who presented a management problem and were resistant to rehabilitative measures were given 1 mg. of reserpine by mouth daily. After 3 months of treatment all were quieter and less hyperactive, while 3 of them showed a very marked improvement in behaviour. *P. Cassar*

Dermatology

1044. Sulfhydryl Groups and Disulfide Linkages in Normal and Pathological Keratinization

E. J. Van Scott and P. Flesch. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **70**, 141–154, Aug., 1954. 4 figs., 32 refs.

The authors have studied, at the University of Pennsylvania, Philadelphia, the chemical changes which occur in keratinization, one of the most characteristic of which involves the sulphur-containing amino-acids. Keratin has been divided into two types, "soft" and "hard", the soft variety (as represented in epidermal keratin and the medulla of the hair shaft) desquamating continually or fragmenting easily, while the hard variety (nails and the cortex of the hair) is a rigid structure. Most of the sulphur in keratin is in the form of cystine, and the disulphide bridges of cystine (generally assumed to result from oxidation of the sulphydryl groups of cysteine) account for much of the stability and chemical resistance of keratin. One of the features of sulphur metabolism which distinguishes hard keratins from soft keratins is an increase in the cystine content which takes place during the course of keratinization.

In a large number of samples of keratin and epidermis obtained from healthy subjects and from patients with various skin diseases the authors found significant amounts of sulphydryl in all types of keratin examined and showed that, while there was a diminution in the sulphydryl content coincident with keratinization, the disulphide concentration of the stratum corneum remained essentially the same as that of the stratum Malpighii. Thus they believe that epidermal keratinization starts in the depth of the Malpighian layer and that conversion of sulphydryl to disulphide does not occur above this level.

In many types of pathological keratinization the sulphydryl and disulphide contents of the horny scales were found to deviate from the normal, the most pronounced —though apparently not specific—aberration being the greatly increased sulphydryl content of psoriatic scales, this being an expression of an increased rate of keratinization. In ichthyosis the sulphydryl and disulphide values were normal. The results are discussed at some length, and the methods of examination described in detail.

E. W. Prosser Thomas

1045. Nature and Functions of the Papillary Ridges of the Digital Skin

N. Cauna. *Anatomical Record* [*Anat. Rec.*] **119**, 449–468, Aug., 1954. 38 figs., 11 refs.

In this report from the Medical School of King's College (University of Durham), Newcastle upon Tyne, the author discusses the nature and functions of the ridges of the digital skin and describes the results of investigations into their relation to tactile function. The material was obtained from 85 individuals of both sexes ranging from a foetus of 28 mm. length to an adult aged 91. The preparation and staining of serial longitudinal, transverse, and horizontal sections in each case are described in detail.

It was shown that the keratin of the stratum corneum is of two types—a hard type in the grooves, providing a framework or skeleton for the epidermis, and a softer type on the projecting papillary ridges covering the underlying touch receptors. These are also of two types, the first being Meissner's corpuscles, over which the epidermis is raised to form the dermal papillae which provide the first points of contact of the papillary ridge. These corpuscles were shown to be selective touch receptors, pressure coinciding in direction with the axis of the corpuscle causing maximum stimulation, and oblique pressure stimulating only a proportion of the nerve endings. These receptors thus appear to be primarily concerned with tactile discrimination. The deep surface of the papillary ridge sends longitudinal epidermal folds of two types into the corium, one in the midline carrying the sweat passages and known as the intermediate ridge, and the other corresponding to the surface grooves and known as the limiting ridges. The intermediate ridge is embedded in loose connective tissue, and its deep surface is in contact with the second type of touch receptor, the epidermal nerve endings (Merkel's disks). The intermediate ridge follows the movement of the papillary ridge and acts as a lever, amplifying touch stimuli in transmitting them to the underlying receptors. This type of receptor can thus be stimulated equally well from different parts of the surface of the papillary ridge and is primarily concerned with tactile acuity rather than discrimination. Developmental studies and comparative anatomy show that the intermediate ridge can be regarded as the primitive touch receptor mechanism common to many mammalian pads, while the sweat glands, surface ridge, and Meissner's corpuscles represent gradual improvements added to this primitive structure during the process of evolution.

[The paper is illustrated with a series of excellent photomicrographs describing the anatomical points discussed.]

Benjamin Schwartz

1046. Malignant Atrophic Papulosis: a Fatal Cutaneo-intestinal Syndrome

R. Degos. *British Journal of Dermatology* [*Brit. J. Derm.*] **66**, 304–307, Aug.–Sept., 1954. 6 refs.

The author presents a study of the rare condition originally described as "atrophic papulo-squamous dermatitis"—subsequently changed to "malignant atrophic papulosis" to emphasize the fatal prognosis—based on 5 cases reported since 1942. This disease is manifested clinically by papules rarely exceeding 10 mm. in diameter and with a whitish, depressed centre, circular in the earlier stages and later becoming irregular. More recent papules have a margin covered with telangiectases. Scarring does not occur. Palms, soles, and mucous

membrane of the mouth and nose are not affected. During the later stages abdominal symptoms occur, characterized by intense pain and vomiting followed by signs of intestinal obstruction.

In all the 5 cases reviewed the acute abdominal syndrome ended fatally in a few days. The epidermal lesions showed no inflammatory changes; only necrotic areas and thrombosis were observed, with hyaline degeneration of the vessel walls. The intestinal lesions also included vascular thrombosis and necrotic areas, but again inflammatory infiltration was absent.

The author is of the opinion that the syndrome is not related to thromboangiitis obliterans, in view of the limitation of the vascular changes to the small vessels, and has not an allergic basis. *Kate Maunsell*

1047. **Erythromycin in Treatment of Dermatoses. Report of 1,695 Patients**
H. M. Robinson, I. Zeligman, R. C. V. Robinson, M. M. Cohen, and A. Shapiro. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **70**, 325–330, Sept., 1954. 5 refs.

In this paper from the University of Maryland School of Medicine, Baltimore, the results are reported of the use of erythromycin in various dermatoses. In 681 cases the antibiotic was given by mouth as enteric-coated tablets in a daily dosage of 800 mg. A large variety of conditions were treated and those due to pyogenic organisms responded well. There was rapid involution of the lesions in 13 out of 14 cases of granuloma inguinale, and the authors believe that the drug was of value in the treatment of erythema multiforme [the natural history of this condition makes results such as these, with no control series, open to doubt]. Symptoms of gastrointestinal disturbance developed in 34 patients while under treatment.

In 1,014 cases local application of 1% erythromycin in a base of oil and soft paraffin was tried. This ointment proved beneficial in various pyogenic infections, including impetigo, ecthyma, and sycosis, as well as in some secondarily infected conditions. No adverse reactions were observed. *S. T. Anning*

1048. **The Interpretation and Importance of Needle Biopsy of the Liver in Certain Dermatoses.** (Significato ed importanza dell'agobiopsia epatica in alcune condizioni patologiche della cute)
M. Dogliotti, M. Banche, and G. C. Angela. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] **95**, 321–376, July–Aug., 1954. 85 figs., bibliography.

The authors, working at the Institute of Clinical Dermatology, University of Turin, point out that hepatic insufficiency, resulting in failure of detoxication, may allow allergens absorbed from the alimentary canal to penetrate into the blood stream; thus sensitization may occur and cause urticaria, angioneurotic oedema, or pruritus, according to the chronicity of the process. It is therefore suggested that a reciprocal relationship between liver disease and skin lesions may exist.

In an attempt to confirm this hypothesis, the authors investigated 41 patients with various skin conditions by means of liver biopsy and the following liver function tests: cephalin–cholesterol flocculation, thymol turbidity, zinc sulphate and cadmium sulphate reaction, and Walderström turbidity; they believe this is the first reported attempt systematically to correlate liver biopsy with skin disease. The technique employed, which followed that of Iversen and Roholm (*Acta. med. scand.*, 1939, **102**, 1), is described in detail; the lack of parallelism between the results of liver function tests and biopsy findings is discussed with reference to the findings of various other workers

Of 14 cases of eczema, liver function tests gave abnormal results in 4, but histopathological changes of a toxic nature were present in 12 cases, consisting in vacuolation of liver cells, degenerative changes in the nuclei, focal necroses, and more or less localized fatty infiltration. In 9 cases of psoriasis of varying type liver function tests suggested liver dysfunction in only 2 instances, whereas histopathological changes were present in 8 cases, being mild in 2 cases and moderate in 5, and resembling periportal fatty infiltration with small areas of necrosis; the 8th case was severe and showed connective-tissue changes suggestive of portal cirrhosis. In 3 cases of bullous pemphigus evidence of disturbed liver function was correlated with the histological findings, which were characteristic of toxic or viral infection, although against this was the presence of severe fatty infiltration and the absence of necrosis. One case of mycosis fungoides showed signs of hepatic parenchymal damage similar to that seen in subacute hepatitis. Further single cases are described. The authors attempt to correlate the changes in the liver with different types of skin disease. *Ferdinand Hillman*

1049. **So-called "Lipomelanotic Reticulosis" of Pautrier–Woringer**
U. W. Schnyder and C. G. Schirren. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **70**, 155–165, Aug., 1954. 7 figs., 24 refs.

There has been much confusion about the condition described and named "lipomelanotic reticulosis" by Pautrier and Woringer in 1932 (*Bull. Soc. franç. Derm. Syph.*, **39**, 947). Recently, at the University Dermatological Clinic, Zürich, the authors had the opportunity of studying 7 patients with enlarged lymph nodes in conjunction with extensive skin affections, including erythrodermata secondary to contact eczema or of unknown causation, generalized recurrent contact eczema, and generalized lichen ruber planus. Histologically, the nodes showed a granulomatous reticulosis of the basic lymph tissue, with inclusions of fat and melanin, the changes being chiefly restricted to the cortex of the node.

The authors believe—as did Pautrier and Woringer—lipomelanotic reticulosis to be a nonspecific reaction of the basic cortical lymph tissue to various inflammatory dermatoses. They discuss the histological differential diagnosis from other granulomatous lymph-node affections, such as Hodgkin's disease, mycosis fungoides, and Brill–Symmers disease (giant follicular lymphoblastoma), for all of which it has been mistaken. They suggest the original name be revived. *E. W. Prosser Thomas*

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

1050. **Oxygen Studies in Retrolental Fibroplasia. IV. Clinical and Experimental Observations**
A. PATZ. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **38**, 291–308, Sept., 1954. 23 figs., 25 refs.

This article from the District of Columbia General Hospital, Washington, gives further support to the now generally accepted view that retrolental fibroplasia is largely an oxygen-induced disease. In it the author reports observations on human premature infants and further experimental work on animals which confirm the results of previous workers who showed that high oxygen concentrations led to (1) early retinal vasoconstriction; and later (2) abnormal capillary proliferation on the retinal surface and into the vitreous. The latter changes in the eye of the young animal are analogous to early human retrolental fibroplasia, and were observed both during oxygen administration and more markedly on withdrawal of oxygen. Retinal detachment, however, resulted in only 2 cases (both in puppies).

The author advances the theory that with high oxygen concentrations in the choroid oxygen diffuses to the retina and there inhibits the principal stimulus for growth of the retinal circulation, namely, a relative oxygen deficiency. He stresses the danger to premature infants of unrestricted oxygen therapy, and points out the absolute necessity of restricting its use to the minimum concentration (less than 40%) for the shortest possible period. *C. A. Brown*

1051. **The Incidence and Severity of Retrolental Fibroplasia in Relation to Possible Causative Factors. Part I. Observations on the Occurrence of Retrolental Fibroplasia. Part II. Studies of the Relationship of Retrolental Fibroplasia to Degree of Prematurity, Oxygen Therapy, General Health, and Date of Birth of Premature Infants**
L. ZACHARIAS, W. E. REYNOLDS, J. F. CHISHOLM, and M. J. KING. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **38**, 317–336, Sept., 1954. 3 figs., 48 refs.

The authors review all cases of retrolental fibroplasia seen at Boston Lying-In Hospital in the two periods 1938–48 and 1949–52. By statistical analysis they show that birth weight and gestational age varied inversely with the incidence and severity of retrolental fibroplasia, whereas the duration of oxygen therapy and the length of stay in the hospital varied directly with the incidence and severity of the disease. A reduction in the severity of the cases seen in 1949 may have been related to the type of incubator then introduced, that is, one which gave a lower concentration of oxygen.

By comparing the figures for the incidence and severity of the disease in the period 1949–50 (" uncontrolled oxygen ") with those for the period 1951–2 (" controlled oxygen ") the authors deduce that the duration of oxygen therapy is not a major, or even a causal, factor in the disease. They remark that oxygen concentration [for which no figures are given, but flow-rates of 3 to 6 litres per minute were used] may be more important than duration of therapy.

[It is now generally agreed that oxygen concentrations of over 40% should not be given.] *C. A. Brown*

1052. **The Therapeutic Possibilities of Carbon Dioxide in the Prevention of Retrolental Fibroplasia**
E. G. FORTIER. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **38**, 342–348, Sept., 1954. 34 refs.

Exposure to a high concentration of oxygen is now considered to be the biggest single factor in the aetiology of retrolental fibroplasia. Since the vasomotor development in premature infants depends on local vascular stimulation rather than on central control from the medulla, the vasoconstrictive effects of high concentrations of oxygen may be explained by their direct effect on local vessels through disturbance of the equilibrium between oxygen and carbon dioxide in the plasma, the high oxygen level resulting in a relative carbon dioxide deficit. The author therefore makes a plea for the use of lower oxygen concentrations in the treatment of premature infants, and for the addition of a non-toxic proportion of carbon dioxide in an effort to eliminate the vasoconstrictive effects of oxygen. *C. A. Brown*

1053. **Increased Plasma Bilirubin in Newborn Infants in Relation to Birth Weight**
B. H. BILLING, P. G. COLE, and G. H. LATHE. *British Medical Journal* [*Brit. med. J.*] **2**, 1263–1265, Nov. 27, 1954. 3 figs., 14 refs.

The relation between birth weight and the plasma bilirubin level of newborn infants was investigated at Queen Charlotte's Maternity Hospital, London. A total of 49 infants weighing at birth 2·75 to 10·24 lb. (1·2 to 4·6 kg.) were divided into 8 groups, the average body weight of successive groups increasing by 1 lb. (0·45 kg.). The infants in the first 3 groups, totalling 19, were premature—that is, they weighed 5·5 lb. (2·5 kg.) or less; the infants in the remaining 5 groups were regarded as normal. For the most part the plasma bilirubin level was estimated daily by van den Bergh's diazo technique on 0·05 to 0·2 ml. of plasma from blood taken by heel-prick with heparin or oxalate. The type of bile pigment in the plasma was determined chromatographically on more than 40 samples from 10 infants in whom the plasma pigment concentration was over 7 mg. per 100 ml. In every instance the pigment behaved on the chromatogram like bilirubin.

The investigation showed that a great excess of bile pigment was characteristic of small newborn infants; of 11 babies weighing less than 4½ lb. (2 kg.) at birth, 9 had a plasma pigment concentration of over 12 mg. per

100 ml., the concentration being 15 mg. per 100 ml. or more in 5 of them. The tendency for a low birth weight to predispose to a high plasma pigment content held throughout the range of birth weights from 3 to 9 lb. (1·4 to 4 kg.). The time taken to reach the maximum plasma pigment concentration and the time required for the level to return to normal were more prolonged in the smaller infants than in the bigger ones, showing that the tissues of small infants are exposed to higher concentrations of bile pigment for longer periods than are those of larger babies. The view is expressed that the reduced excretory capacity of the liver responsible for the accumulation of bile pigment in the plasma may be due to a specific defect concerned with the immediate metabolism of bilirubin. This view finds support in the fact that minimal amounts of direct-reacting bile pigments are present when there is a high concentration of plasma bilirubin. The authors do not regard "physiological" jaundice as a physiological adjustment to extra-uterine life, but rather as a result of incomplete development of the liver before birth. *David Morris*

1054. **Treatment of Erythroblastosis Fetalis by Exchange Transfusion. Statistical Analysis of Results**
A. S. Wiener, I. B. Wexler, and G. J. Brancato. *Journal of Pediatrics* [*J. Pediat.*] **45**, 546–568, Nov., 1954. 48 refs.

The authors review their experience with exchange transfusion in the treatment of erythroblastosis foetalis, and briefly outline their concept of the rationale of the treatment. For the sake of simplicity Rh_0 sensitization only is discussed, but it is pointed out that "the same principles apply in cases of ABO hemolytic disease, and isosensitization to Hr, Kell, and other blood factors". Death from erythroblastosis is due not only to anaemia but also to damage to the tissues caused, in the authors' opinion, by the intravascular conglutination of antibody-coated erythrocytes under the influence of an accessory factor which is probably not fully developed until after birth. Replacement of the infant's erythrocytes must therefore be carried out as soon as possible, 85% replacement, obtained by giving about twice the infant's blood volume, probably being adequate. In experiments with various methods and quantities the authors found that transfusion of a large volume (1 litre) of whole citrated blood caused death through over-loading, while transfusion of a small volume of packed erythrocytes (haematocrit 0·75) gave rise to neurological symptoms, and concluded that the best results were obtained with a compromise between these two extremes. They concentrate the donor's blood by withdrawing plasma until the haematocrit level is 0·5, the volume given being about 400 ml.; they do not give any excess of blood over the volume withdrawn. A second transfusion is sometimes necessary.

For the assessment of results the authors use the maternal antibody titre at term (estimated by the albumin–plasma conglutination method) as the index of severity, dividing their cases into those in which the titre was more than 8 units and those in which it was less than 8. Out of 28 babies in the former category who were given simple transfusion or expectant treatment, 13 either died or developed neurological complications, whereas out of 154 treated by exchange transfusion, 24 died or developed neurological complications. In the low-titre group, as would be expected, there was little disease and no significant difference between the results of the different methods of treatment.

There are few clear-cut indications for exchange transfusion, but it is recommended that if the maternal antibody titre is above 8 units and the baby is Rh positive, transfusion should be performed even if the baby is apparently quite well. If the maternal antibody titre is low, transfusion is indicated: (1) if the icterus index of the cord blood is 20 units or over; (2) if the infant's haemoglobin concentration is less than 15 g. per 100 ml.; or (3) if the result of the direct antiglobulin test is strongly positive. A history of erythroblastosis in a previous infant or of transfusion in the mother is an additional indication. Where Rh sensitization is diagnosed during pregnancy the time of delivery should be such as to avoid both the hazards of prematurity and the dangers of the rising antibody titre in the last weeks of pregnancy. Delivery per vaginam 2 weeks before term is probably the ideal to aim at. *J. G. Jamieson*

1055. **Longitudinal Study of the Incidence of Central Nervous System Damage following Erythroblastosis Fetalis**
M. H. Jones, R. Sands, C. B. Hyman, P. Sturgeon, and F. P. Koch. *Pediatrics* [*Pediatrics*] **14**, 346–350, Oct., 1954. 5 refs.

At the Children's Hospital (University of Southern California), Los Angeles, 100 erythroblastotic infants, in all of whom the Coombs test gave a positive result, were studied for periods varying from 6 months to 5 years. Although a fair degree of correlation was found between the presence of early signs of damage to the central nervous system and of subsequent motor or neuromuscular handicap, the severity of the latter was not related to the severity of the former. Whereas all the 6 patients with definite signs of cerebral damage in the neonatal period proved to have a neuromuscular abnormality in later childhood, 3 of the 76 whose central nervous system was regarded as normal in the neonatal period were found to have definite abnormalities later. At the later examination 15 of the 100 had some neuromuscular handicap, which was regarded as "mild" in 2 cases, "moderate" in 6, and "severe" in 7. [The treatment given to these patients in the neonatal period is not stated.] *M. Baber*

1056. **Non-surgical Treatment of Unilobar Obstructive Emphysema of the Newborn**
H. W. Korngold and J. M. Baker. *Pediatrics* [*Pediatrics*] **14**, 296–304, Oct., 1954. 16 figs., 11 refs.

The authors describe 2 cases in which newborn infants were successfully relieved of unilobar obstructive emphysema by selective decompression, and review 22 similar cases reported in the literature, 18 of which were cured surgically. In half the cases no cause was found for the bronchial obstruction. In their two cases the authors

believe that the involved bronchus was partially obstructed by kinking, due to overdistension of the lobe and herniation through the mediastinum, and by retention of viscid secretions. In both cases on the third day of life an 18-gauge needle was introduced into the affected lobe and 200 to 300 ml. of air aspirated with immediate clinical improvement, which was followed some hours later by the occurrence of a tension pneumothorax requiring further aspiration 2 or 3 times in the next 24 hours, by which time the needle-wound in the emphysematous lobe had healed. The babies were clinically normal 6 and 5 months later respectively.

The clinical picture in both cases was of dyspnoea, wheezing, and choking shortly after birth, with rapid, laboured breathing, retraction of the costal arch, diminished breath sounds over the affected lobe, and occasional expiratory wheezing. Radiographs of the chest showed emphysema of the involved upper lobe, which filled the entire hemithorax, with compression of the lower lobe, mediastinal shift, and herniation through the anterior mediastinum. The differential diagnosis includes pneumomediastinum (in which the lung fields show no change and the antero-posterior view usually shows no abnormality), atelectasis with compensating overfilling, and lung cysts. The authors recommend non-surgical treatment when the emphysema is newly established and reversible, and possibly in later cases to improve the patient's condition before operation.

A. W. Franklin

1057. **Snuffles in the Newborn. Frequency, Aetiology, and Natural History**
J. APLEY, B. LAURANCE, and I. F. MACMATH. *Lancet* [*Lancet*] **2**, 1048–1051, Nov. 20, 1954. 7 refs.

A total of 99 infants who developed snuffles in the first month of life were observed, mostly in maternity units of hospitals in the Bristol area, until the condition cleared up. Snuffles, which is here defined as nasal obstruction or discharge in infancy, was observed in about 2·6% of infants born in 4 maternity units. Birth weight did not appear to influence the incidence, and there was no seasonal variation. The condition usually started before the 12th day of life; it seldom lasted longer than a week, but if it did, it tended to continue for weeks or months. The nasal discharge was usually serous, sometimes purulent, but rarely blood-stained. In a few cases nasal obstruction preceded the appearance of a discharge. The common complications were mouth-breathing and mild feeding difficulties. "Suffocative rhinitis" occurred in 4 cases, the infants being seriously ill, with complete blockage of the nostrils by tenacious exudate. Severe lung infection was present in 5 infants, and persistent collapse of a lobe occurred in one.

The cause of the snuffles was far from clear. In many cases no organisms could be cultured from nasal swabs; in most of the other cases the organisms did not differ from those found in unaffected infants. In a very few instances the infant was considered to have contracted coryza from adult contacts. No case of congenital syphilis or of nasal choanal atresia was detected, and there was no evidence of allergy.

The authors conclude that snuffles is seldom due to infection. They suggest that variations in the quantity or viscosity of mucous secretions in infancy may play a part in the aetiology of this condition. The essential in treatment is maintenance of the patency of the airway, and they endeavour to re-establish nasal breathing by persuading the mother to hold the infant's mouth closed as often as possible and for increasingly long periods.

[At first sight it is surprising that no mention is made of another Bristol report, that of Woods on the common cold in infancy (*Med. Offr*, 1951, **86**, 247), but the two papers have only a little common ground.]

Mark S. Fraser

1058. **Epidemiological Observations on Interstitial Pneumonia of the Newborn.** (Epidemiologische Beobachtungen bei der frühkindlichen interstitiellen Pneumonie) G. A. VON HARNACK. *Annales paediatrici* [*Ann. paediat. (Basel)*] **183**, 224–240, Oct., 1954. 5 figs., 16 refs.

The author reports an increase in the incidence of interstitial pneumonia among newborn babies in Hamburg during the period 1950–4 and reviews 191 cases, of which 113 occurred in girls and 78 in boys. The birth weight was 2·5 kg. or more in 42% of cases. The mortality among the boys was 38·7% and among the girls 40·7%. The disease showed no seasonal preference. The age at onset ranged from 5 weeks to 7 months, but 83·5% of the cases occurred in infants between the ages of 9 and 16 weeks. At the onset of the disease there was a prodromal period extending over several days before tachypnoea set in. In a few cases radiological changes were noticed before the appearance of tachypnoea. The incubation period appeared to vary between one and 2 months, the shortest observed being about 22 days and the longest 78 days. In 7 out of 14 pairs of twins, both were affected. It was noted that where only one twin was affected it was not always the smaller of the two, nor was the smaller twin more likely to die when both were affected. Among 85 babies in two wards who were exposed to the same risk of infection, only 15 (18%) became infected. It was concluded that the most important cause of spread of the infection was the transfer of babies during the incubation period from hospital to hospital or from hospital to home or vice versa. The author is of the opinion that apart from rest and treatment with oxygen there is no reliable therapeutic agent.

Franz Heimann

CLINICAL PAEDIATRICS

1059. **A Follow-up of Cases of Plumbism in Children**
D. A. HENDERSON. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 219–224, Aug., 1954. 1 fig., 14 refs.

Lead poisoning was extremely common in Queensland until the use of lead paint on veranda railings and other structures was prohibited by law. Although this legislation was passed in 1922 it was not until the late 1930's that plumbism in children ceased to be a problem. The author reports a follow-up investigation of 401 children treated for plumbism at the Hospital for Sick

Children, Brisbane, between 1915 and 1935. Of this number 165 were known to be dead, 187 were alive, and 49 were untraced. According to the death certificates renal or vascular disease was the cause of death in 108 of the 165 fatal cases, nephritis or nephrosclerosis being given as the immediate cause in 105 of them. Of the patients who were still alive 101 were followed up, and of these, 17 suffered from hypertension and albuminuria and 3 had hypertension alone.

The author states that so far as could be ascertained the original diagnosis of plumbism was probably correct in the majority of cases. *Winston Turner*

1060. **Treatment of Juvenile Melanomas and Malignant Melanomas in Children**

H. E. McWHORTER, F. A. FIGI, and L. B. WOOLNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 695–698, Oct. 16, 1954. 16 refs.

This paper from the Mayo Clinic presents some further details, especially concerning treatment, of 16 previously reported cases of melanoma in childhood (*Cancer (N.Y.)*, 1954, **7**, 564; *Abstracts of World Medicine*, 1954, **16**, 357). The tumours in 11 of the cases were benign and considered by the authors to be examples of "juvenile" melanomata and in 5 cases they were malignant. A study of the literature revealed that a number of workers had described a type of melanoma occurring in children which histologically appeared to be malignant but which followed a benign course. The present authors believe, however, that there are histological features which permit differentiation of the truly benign melanomata from the few which are malignant.

The juvenile melanomata were seen in children between 12 months and 9 years of age, and about equally in boys and girls. The lesions, which were 4 to 10 mm. in diameter, occurred most frequently on the head and face and less commonly on the limbs, and were slightly raised above the surface. The rate of growth was slow, most of the lesions having been present for a year before excision. Microscopically, the naevus cells were large and of equal size. No anaplastic changes were seen. Although these lesions were treated by local excision (4 patients received irradiation therapy as well) there was no recurrence over a follow-up period varying from 3½ to 23½ years.

The malignant melanomata occurred in children between 4 and 11 years of age—3 boys and 2 girls—and in 4 cases were situated on the face and ears (the site of the lesion in the fifth case is not recorded). Three children with palpable metastases in the regional lymph nodes died with telemetastases within a year, in spite of excision and dissection or irradiation of the lymph-node metastases. In the remaining 2 children there was histological evidence of lymphatic metastases; one died 6½ years after local excision and regional irradiation, there being melanomatous deposits in the cervical lymph nodes; the other was alive 21 years after treatment. Histologically all the lesions showed malignant characteristics, the naevus cells being irregular in size and shape and in the arrangement of the nuclei and chromatin. The nucleoli were abnormally large and the cells contained melanin. The histological findings were similar to those observed in malignant melanomata in adults.

In the treatment of juvenile melanomata the authors recommend wide local excision of the "junctional tissue"—tissue between the lesion and the normal skin in which extension of the lesion can often be seen microscopically. In cases of malignant melanoma local excision should be as wide as is practicable, the defect being covered with a split skin graft. Palpably enlarged regional lymph nodes should be excised by block dissection, but if the regional nodes are not enlarged an expectant attitude should be adopted. The authors quote the findings of Allen and Spitz (*Cancer (N.Y.)*, 1953, **6**, 1; *Abstracts of World Medicine*, 1953, **14**, 160) that a relatively high proportion (68·3%) of their patients with malignant melanoma who survived 5 years or longer were treated by wide local excision without dissection of the regional lymph nodes; in another 13% of cases dissection of regional nodes was performed but no metastatic deposits were found on histological examination.

Charles P. Nicholas

1061. **Purulent Meningitis in Infants and Children. A Review of 409 Cases**

E. S. SMITH. *Journal of Pediatrics* [*J. Pediat.*] **45**, 425–436, Oct., 1954. 7 figs., 18 refs.

Haemophilus influenzae is the most common cause of meningitis in children; *Escherichia coli* is the most common cause in the neonatal period. More cases of meningitis occur in the first month of life than in any other month; almost one-half of the cases occur in the first year of life. The mortality in meningitis decreases sharply after the first month of life. Prognosis is most favourable in *H. influenzae* meningitis and least favourable in tuberculous and *Esch. coli* meningitis. A high incidence of complications is associated with pneumococcal meningitis. Subdural effusion secondary to meningitis is not a common or serious complication.—[From the author's summary.]

1062. **Surgical Treatment of Pulmonary Cysts in Infancy. Report of Three Cases**

H. SWAN and G. E. ARAGON. *Pediatrics* [*Pediatrics*] **14**, 651–658, Dec., 1954. 7 figs., 12 refs.

1063. **The Treatment and Prevention of Epidemic Infantile Diarrhea due to *E. coli* O-111 by the Use of Chloramphenicol and Neomycin**

W. E. WHEELER and B. WAINERMAN. *Pediatrics* [*Pediatrics*] **14**, 357–363, Oct., 1954. 2 figs., 6 refs.

Treatment both with chloramphenicol and with neomycin was successful in combating toxaemia and reducing mortality almost to *nil* in a severe outbreak of enteritis due to *Bacterium coli* O-111 at the Children's Hospital, Columbus, Ohio, but chloramphenicol was much less effective than neomycin in causing the disappearance of the organisms from the stools. This was due to the emergence of chloramphenicol-resistant strains in a high proportion of cases, with the result that an attempt to prevent cross-infection by the prophylactic use of this drug failed. *M. Baber*

Medical Genetics

1064. **Familial Occurrence of Migraine Headache. A Study of Heredity**
H. GOODELL, R. LEWONTIN, and H. G. WOLFF. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. Chicago*)] **72**, 325–334, Sept., 1954. 2 figs., 12 refs.

Adequate replies to a request for a detailed family history in respect of migraine were received from 65 patients treated for migrainous headache at the New York Hospital, and from 54 private patients of one of the authors. In all, 343 affected relatives were traced through the 119 index cases, but only 34 of these relatives and the 65 hospital out-patients were interviewed personally by the authors; there was no control group. Migraine is loosely defined as headache, unilateral in onset but sometimes becoming generalized, associated with anorexia, nausea, vomiting, photophobia, and changes in mood, the attacks lasting from less than one hour to several days. In the cases treated the course was shortened by giving ergotamine tartrate.

Of the propositi, 48 were males and 71 females and their ages ranged from 16 to 65 years. The numbers of migrainous patients having 0, 1 to 3, 4 to 7, and 8 to 19 affected relatives were respectively 20, 66, 22, and 11, while two generations were reported as being affected in 43 instances and three or more generations in 52. In the whole series the incidence of migraine among children having respectively neither parent, one parent, and both parents affected was 28·6, 44·2, and 69·2%. The statistical analysis of these and other reported figures is discussed. From the results of this study the authors postulate that the inheritance of the migraine trait is through a recessive gene with approximately 70% penetrance. The alternative, that inheritance is through a dominant gene with partial penetrance is mentioned, but cannot of course be tested. *R. H. Cawley*

1065. **Dystrophia Myotonica and the Occurrence of Congenital Physical Defect in Affected Families**
J. E. CAUGHEY and J. BARCLAY. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 165–170, Aug., 1954. 6 figs., 22 refs.

The authors report an investigation into the incidence of congenital physical defects in other members of the family of a patient suffering from dystrophia myotonica. In all, 10 such cases were discovered in 5 families, which are described in detail, with genealogical trees showing the relationship to the myotonic patient.

One patient with dystrophia myotonica had 2 children both of whom had cleft palate and hare-lip. Another had one child who was educationally retarded, a second child with congenital cataract, and a third with bilateral club foot. In a 3rd case the patient's brother suffered from spastic paraplegia, while a 4th patient had 2 nieces also with spastic paraplegia. The 5th patient had a son who, in addition to dystrophia myotonica, had bilateral congenital inguinal hernia and club foot. The authors were unable to obtain comparable figures for the incidence of such congenital deformities in unselected families or in the general population, and therefore, in view of the small number of cases involved, draw no definite conclusions. But they point out that the incidence of defects seemed to be higher in the offspring, and particularly in children of the women, of the " dystrophic generation " than in sibs of the patients. *C. O. Carter*

1066. **Congenital Hereditary Hematuria**
G. C. REYERSBACH and A. M. BUTLER. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 377–380, Sept. 2, 1954. 2 figs., 19 refs.

The authors describe 8 cases of congenital hereditary haematuria seen during the last 18 years. In 7 of these albuminuria and haematuria were present at all times, while in the 8th they were found only intermittently. All the cases were recognized in infancy or childhood and several of them have been followed up for periods of 10 to 20 years. All the patients grew and matured normally, but 3 of them, all boys, had nerve deafness, which seems to be an associated part of the syndrome. Generally males are more seriously affected than are females, as was the case in this small series.

The 8 patients belonged to four separate, unrelated families of Anglo-Saxon descent. The familial distribution in these families and also in a number of families previously reported in the literature is consistent with the hypothesis that the syndrome is inherited as a Mendelian dominant character, with some irregularity of expression. The importance of distinguishing the condition from acute or chronic glomerulonephritis is pointed out. No specific therapy that modifies the haematuria or course of the disease is known. *Harry Harris*

1067. **A Contribution to the Genetics of Gargoylism**
R. C. CUNNINGHAM. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 191–195, Aug., 1954. 4 figs., 15 refs.

The fundamental defect in gargoylism is twofold—a chondro-osseous dystrophy involving the skull, spine, ribs, and long bones, and storage deposition of an abnormal macromolecular substance in the reticulo-endothelial system and in parenchymatous and connective tissue. The condition is hereditary, but the mode of inheritance is uncertain, some pedigrees pointing to a single recessive autosomal gene and others to a sex-linked recessive gene.

An English family is described in which there occurred 12 instances of gargoylism in 3 generations. The author was able to examine 2 of the patients and get reliable descriptions of the other 10. The pattern was that of sex-linked recessive inheritance. As in other sex-linked recessive pedigrees, the patients' corneae were not affected. In this family the patients were consistently idiots or imbeciles and their skin was unaffected.
C. O. Carter

Public Health

STATISTICS

1068. Calcium Chloride and Adrenaline as Bronchial Dilators Compared by Sequential Analysis

G. S. KILPATRICK and P. D. OLDHAM. *British Medical Journal* [*Brit. med. J.*] **2**, 1388–1391, Dec. 11, 1954. 3 figs., 22 refs.

The authors report the results of a clinical trial carried out by the M.R.C. Pneumoconiosis Research Unit at Llandough Hospital, Cardiff into the relative effectiveness of inhalations of aerosols of calcium chloride and of adrenaline in relieving bronchial spasm. But this was a clinical trial with a difference. Most medical men are now familiar with the classic type of trial based on the random allocation of patients to groups receiving different treatments, where the size of the groups is decided (often loosely) in advance. The "sequential" type of trial, which has been in process of development outside the medical field during the past ten years and which the authors claim the distinction of applying for the first time in a therapeutic trial, involves no such predetermination of numbers. Continuous analysis of the results of different treatments as the trial proceeds permits it to be brought to a close as soon as the numbers are large enough to enable a decision to be reached about the existence or non-existence of a statistically significant difference between them. Armitage (*Quart. J. Med.*, 1954, **23**, 255) in an admirable review of the methodology of this type of trial postulated three conditions for its application: (1) it must be possible to select one characteristic of much greater importance than any other by which the results of treatment can be compared; (2) it must be administratively possible to conduct the trial without previously deciding its ultimate length; and (3) the time required to assess the response to treatment must not be long.

In this trial the characteristic selected as the principal measure of the bronchodilator effect of calcium chloride and adrenaline was the expiratory flow rate (E.F.R.), the determination of which takes only a few seconds, and no limit was set to the length of the trial—patients with bronchial spasm of diverse aetiology were accepted from the Pneumoconiosis Unit's ward and the general wards as they became available. Thus Armitage's conditions were all satisfied. Each patient received a 15-minute inhalation of an aerosol of 3 ml. of a solution of either calcium chloride (20%) or adrenaline (1 in 200) in the morning and of the alternative drug in the evening, the particular drug used on each occasion being unknown to both patient and observer. The E.F.R. was measured before and immediately after each inhalation, the gain in E.F.R. resulting from the inhalation of calcium chloride in the first 4 cases being 0·2, *nil*, −1·1, and −4·8 litres per minute respectively, whereas the corresponding figures for adrenaline were 9·2, 3·8, 7·6, and 5·8 litres per minute. At this stage sequential analysis of the results permitted the conclusion that calcium chloride had no advantage over adrenaline in the relief of bronchial spasm and the trial was terminated. On repetition of the test on different subjects and using a 10% solution of calcium chloride very similar results were obtained, the trial again being terminated after 4 patients had been treated with both drugs.

It is pointed out that from the type of sequential trial adopted here it was possible to determine only whether calcium chloride was or was not a better bronchodilator than adrenaline, but that the adoption of a slightly different procedure would have enabled the authors to determine whether or not adrenaline was more effective than calcium chloride.

[The authors are to be commended for their initiative in applying the sequential method of analysis in this trial. It clearly has advantages in the investigation of certain types of medical problem, and no doubt much more will be heard of it.] *E. Lewis-Faning*

HYGIENE

1069. Observations on the Disinfection of Hospital Blankets with Quaternary Ammonium Compounds during Laundering

L. STEINGOLD, J. H. F. WOOD, and W. E. FINCH. *Journal of Applied Bacteriology* [*J. appl. Bact.*] **17**, 159–166, Oct., 1954. 17 refs.

In presenting the results of the experimental disinfection of hospital blankets with quaternary ammonium compounds (Q.A.C.), carried out at St. Andrew's Hospital, London, the authors first describe a method for assessing the total viable bacterial content of blankets. In this an area of blanket selected at random is placed over a Petri dish containing a simple nutrient agar medium and a stream of cold air directed on to it for about 5 minutes from a portable hair-drier held about half an inch (1 cm.) above the blanket; successive exposures of 1 minute were also made on the same area of blanket. The air entering the apparatus was filtered through a thin layer of cotton wool between surgical gauze fitted at the intake. The mean colony count obtained from replicate plates after incubation at 37° C. was taken as a measure of the bacterial content of the blanket.

Assessments first carried out on blankets from both medical and surgical wards before and after ordinary laundering showed that ordinary laundering had very little antibacterial effect, but merely redistributed the organisms among the blankets, thus facilitating cross-infection. The incorporation of Q.A.C. in the laundering process—three methods of doing this are described but all three gave closely similar results—resulted in the production of virtually sterile blankets. Further experiments showed that Q.A.C. are adsorbed by blankets and that the amount adsorbed can be controlled by varying the ratio of dry weight of blanket to concentration

of Q.A.C. in the washing solution. Also, whereas wetting untreated used blankets with saline did not lower their bacterial contamination, blankets laundered with Q.A.C., although inevitably becoming contaminated during use, were easily disinfected by mere wetting. This property was retained for at least 14 days, but not after 24 days, from the time of treatment. It is pointed out that Q.A.C. are cationic and therefore incompatible with ordinary soaps and most of the commonly used detergents, which are anionic; the detergent used in this investigation was "lissapol NX", which is non-ionic. Good results were obtained, however, merely by adding Q.A.C. (200 p.p.m.) to the final rinse. *J. Cauchi*

1070. Air Pollution and Bronchitis

J. PEMBERTON and C. GOLDBERG. *British Medical Journal* [*Brit. med. J.*] **2**, 567–570, Sept. 4, 1954. 2 figs., 14 refs.

It has been shown that the crude death rate from bronchitis is correlated with density of population, being least in rural areas and greatest in conurbations, and it is suspected that atmospheric pollution, particularly with sulphur dioxide, plays an important part in this.

From a study of the data available in the Registrar-General's Annual Reviews and figures for atmospheric pollution published by the Department of Scientific and Industrial Research the authors, working at the University of Sheffield, have attempted to throw further light on this problem in respect of the age groups 45–64 and 65+ in 35 county boroughs of England and Wales for the years 1950, 1951, and 1952. The statistical methods employed are described. They showed that there was a moderate degree of correlation between the death rate from bronchitis in males over the age of 45 and the concentration of sulphur dioxide in the atmosphere. There was, however, no significant correlation in regard to women under 65; and no correlation with any other current measure of air pollution such as, for example, suspended solid matter, could be established. As the authors state, the imperfection of the basic data precludes any firm conclusions, but they suggest that atmospheric pollution is probably not a primary aetiological factor in bronchitis, but rather a secondary or aggravating factor. *Scott Thomson*

INFECTIOUS DISEASES

1071. Pulmonary Tuberculosis in a Rural School and Community. A Follow-up Study

G. M. SMITH, M. MACLELLAN, and J. E. HILTZ. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 255–260, Oct., 1954. 1 fig., 1 ref.

This paper is concerned primarily with the results of a 5-year follow-up investigation of cases of pulmonary tuberculosis (including family and school contacts), which were brought to light in 1948 in the Fundy Health Division of the Province of Nova Scotia when a schoolboy was found to be suffering from tuberculous meningitis. The Fundy Health Division, which consists of the fruit-growing Annapolis Valley, has a population, mainly rural, of about 80,000. The inhabitants are mostly of English or Scottish descent, with a low tuberculosis death rate and, judging from the results of tuberculin patch tests, a low infection rate in children —only 5·4% in 1952, the average number of children tested being approximately 1,800 a year.

Since the source of infection of the original case of tuberculous meningitis was not known it was decided to subject the patient's school contacts (34) to the Vollmer tuberculin patch test. Of the 34 contacts, 19 gave a positive reaction to the test. Radiographs showed that 7 of these had a typical primary complex (active), one had a pleural effusion, and one minimal active pulmonary tuberculosis. Examination of home contacts revealed 2 cases of moderately advanced disease, one of pleural effusion, and one of primary active infection. Finally, in a neighbouring village, a cousin of the original patient was found to have moderately advanced tuberculosis [presumably hitherto unsuspected].

At the time of the follow-up investigation 7 of the patients with active tuberculosis had made an uneventful recovery. Of the 14 in whom the response to the patch test had been negative, 7 still gave a negative reaction, 4 gave a positive reaction (one with a radiologically demonstrable focus), and 3 could not be traced. In the intervening years 29 new children had entered the school, but only 7 of these gave a positive reaction to tuberculin, including 6 who were known to be contacts, 2 of them having had primary tuberculosis. The follow-up in the homes and among indirect contacts revealed 2 fresh cases of active disease and 8 new cases of primary infection or re-infection. Altogether the total number of "new cases" of tuberculosis found between 1949 and 1954 was 27, or nearly half of the number of contacts (58) examined.

[It is not, however, quite clear how many of these patients can be considered to have progressive disease: it may be too early to say. But the report shows the value of progressive epidemiological inquiry, especially in a limited rural population. The inclusion of cases of "primary inactive" and other doubtful forms of the disease as "cases of tuberculosis"—an increasingly common practice nowadays—confuses the issue in an otherwise good study.] *R. J. Matthews*

1072. Significance of "Cysts" following Injections of Antigens

V. K. VOLK, F. H. TOP, and W. E. BUNNEY. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1314–1325, Oct., 1954. 4 figs., 7 refs.

It has been observed that in some subjects receiving an injection of an antigen, particularly alum precipitated diphtheria toxoid, a sterile abscess or, as the authors of this paper term it, an antigen cyst, develops. The subjects are those whose immunity to the specific disease is already high, and the appearance of the cyst is evidence that the injection was unnecessary. Such cysts are most frequently seen in subjects with a history of previous inoculation and in inmates of institutions; they appear more often after subcutaneous injection than after an intramuscular injection. *Scott Thomson*

Industrial Medicine

OCCUPATIONAL DISEASES

1073. **Hematological Investigation on Workers Exposed to Manganese Dust**
B. KESIĆ and V. HÄUSLER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 336–343, Oct., 1954. 32 refs.

The authors report, from the Institute of Industrial Hygiene, Zagreb, Yugoslavia, a preliminary investigation into the effect of exposure to manganese oxide dust on the blood cells and haemoglobin level which was carried out on two groups of manganese workers: (1) 16 men suffering from chronic poisoning after prolonged exposure to atmospheric concentrations of 7·5 to 63·3 mg. per c. metre; and (2) 50 miners who were "practically healthy" and who showed no symptoms after exposure to a maximum atmospheric concentration of 8·9 mg. per c. metre. A group of 60 comparable but non-mining subjects from the same area were examined as a control.

In the 16 men with chronic poisoning the range of erythrocyte count (4·1 to 4·6 million) and haemoglobin value (76 to 93%) was considered to be normal for the district. In 4 of these men the leucocyte count was below 5,000 per c.mm., but there was no statistical evidence that this leucopenia could be attributed to exposure to manganese. The 50 miners without symptoms showed a significantly raised mean haemoglobin level (15·03 g. per 100 ml. as against 14·19 g. for the controls), and also a raised erythrocyte count (4·5 million compared with 4·3 million). The only other difference was in the proportion of monocytes, which was reduced to 6·4% in the exposed miners, compared with 7·8% in the controls. The authors conclude that the first phase of exposure to manganese stimulates erythropoiesis and depresses the number of monocytic leucocytes. They saw no evidence of anaemia, as has been reported by other workers. *R. E. Lane*

1074. **Pneumoconiosis from Exposure to Kaolin Dust: Kaolinosis**
K. M. LYNCH and F. A. MCIVER. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 1117–1127, Nov.–Dec., 1954. 7 figs., 3 refs.

Two cases of massive pneumoconiosis due to the inhalation of kaolin dust are described. The authors claim that this is a previously unrecognized form of pneumoconiosis which is distinct from silicosis, and to which the name "kaolinosis" should be applied. Although the pathological and radiological appearances are in general similar to those of massive silicosis, kaolinosis is said to be characterized by massive involvement of the upper parts of the lungs and marked emphysema of those areas in which the air space is not obliterated.

[Massive pneumoconiosis of the type described, due to kaolin, has in fact been described before, by Tara and Trouard-Riolle (*Arch. Mal. prof.*, 1948, **9**, 292), and by Thomas (*Lancet*, 1952, **1**, 133; *Abstracts of World Medicine*, 1952, **11**, 337).] *C. M. Fletcher*

1075. **Pneumoconiosis in the Hard Metal Industry.** (Pneumokoniose in der Hartmetallindustrie)
K. D. LUNDGREN and H. ÖHMAN. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **325**, 259–284, 1954. 9 figs., 14 refs.

The authors describe, from the Karolinska Hospital, Stockholm, an investigation into the incidence of dust disease of the lungs among the workers in five factories where the carbides of the hard metals wolfram (tungsten), titanium, and cobalt are produced. The carbides, having a very high melting point, cannot be processed in a molten state and it is necessary to handle the powdered metals. A brief technical note is given of the processes of production and mixing of these metal powders, and the relevant literature is reviewed.

Out of a total of between 200 and 250 men employed in these works there were 5 cases of severe pulmonary disease, 3 of which were fatal; 4 of the cases are described in detail. The symptoms were an irritating cough, with or without sputum, and marked shortness of breath progressing to dyspnoea and cyanosis. *X*-ray examination showed widespread punctate shadows, sometimes confluent and patchy, but bronchoscopy revealed nothing more than a reddening of the bronchial mucosa with mucus secretion and a diffuse catarrhal bronchitis with no specific signs. In one of the cases this stage was followed by amelioration of the symptoms, which lasted for 3 years, only to be succeeded by rapid deterioration and death. Post mortem the lungs showed a most unusual state of carnification, somewhat similar to the liver in cirrhosis, but in no way resembling the picture of a silicotic lung. In another case necropsy showed only a chronic non-specific interstitial pneumonia. Tests by inoculation of guinea-pig and examination of the sputum were negative for the tubercle bacillus. The symptoms in the 2 non-fatal but severe cases were similar, and in these patients treatment with antibiotics and breathing exercises resulted in a slight temporary improvement, but the dyspnoea and inability to work persisted.

In a study of the dust contamination of the air it was shown that 90 to 100% of the particles were less than 4 μ in diameter. The dust count by the "konimeter" was found to be three times smaller than that obtained by the "impinger", a result attributed to the stronger current of air through the latter device. Of the 200 or so workers exposed to the dust of the hard metals, 54 complained of symptoms such as irritating cough, catarrh, dryness and burning of the throat, and shortness of breath. Only

one of these, a woman, showed radiological signs of lung disease. Some 40 of the workers had eczema, and others gave a history of skin ailments which they attributed to their work. Patch testing with cobalt chloride gave a positive result in 8 cases only, and in a further 6 gave a very doubtful reaction, while all patch tests with wolfram and titanium compounds gave negative results. There was thus no definite correlation between the respiratory and the cutaneous disorders.

In discussion the authors point out that the clinical resemblance to tuberculosis, the absence of specific findings, and the low correlation of duration of employment with incidence of the illness all left the diagnosis unsatisfactory. The problem is discussed, and the possibility of an allergic factor in causation is suggested. Further experiments to determine the precise aetiology are being undertaken. *M. A. Dobbin Crawford*

1076. **Tuberculosis and Coalworkers' Pneumoconiosis**
A. L. COCHRANE. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 274–285, Oct., 1954. 4 figs., 38 refs.

The author traces the development over the last two centuries of the view that coal-dust inhalation in some way modifies the response of the lung to tuberculous infection and draws attention to the change in opinion concerning the prognosis of tuberculosis in coal-miners during the past few decades. The view that mortality from the disease was low among coal-miners was generally accepted in the 18th and 19th centuries, but has now been reversed. He refers to a number of recent epidemiological investigations, and, after quoting contemporary views on the changing relationship between tuberculosis and pneumoconiosis, examines the results obtained in the Rhondda Fach investigation. These showed that possible causal factors of the changed relationship included an occupational factor ("selection") and a significant connexion between certain categories of simple pneumoconiosis and progressive massive fibrosis [for details of which reference should be made to the text].

The author discusses the evidence at some length, and concludes with the hypothesis that "a little coal dust retained in the lungs has a definite therapeutic effect, whereas larger accumulations increase the attack and mortality rates from tuberculosis". [Although this hypothesis is not entirely new, the author's premises and reasoning are interesting.] *R. J. Matthews*

1077. **Silicosis and Polyarthritis.** (Silikose und Polyarthritis)
H. PETRY. *Archiv. für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **13**, 221–236, 1954. 2 figs., 24 refs.

The author was impressed by the frequency with which advanced silicosis appeared to be associated with rheumatoid arthritis in miners attending the Miners' Hospital at Hamm, and set out to determine whether the association was valid. Of 350 patients who had been diagnosed between 1947 and 1953 as having rheumatoid arthritis, 160 had not been exposed to a silicosis hazard. Of the remaining 190, all of them coal-miners, radiographs of the chest showed normal appearances in 61%, silicosis of Stages I and II in 14%, and silicosis of Stages II–III and III [equivalent to pulmonary massive fibrosis (P.M.F.) in the British classification] in 25% (48 cases). The proportion of cases of P.M.F. was thus very much greater than that found in field surveys of working miners in Germany, which is less than 1%. Among 116 arthritic patients with a history of over 15 years' exposure to dust, 43 (37%) had P.M.F., whereas in the general population of German miners with 20 years' exposure and more the proportion is only 6%, while of 100 patients attending the Hamm clinic for conditions other than arthritis who had worked underground for more than 30 years, only 8 had P.M.F. The author concludes that there must be a real association between massive fibrosis and rheumatoid arthritis. This confirms the observations of Caplan *et al.* (*Brit. med. J.*, 1953, **2**, 1231; *Abstracts of World Medicine*, 1954, **15**, 535), in South Wales, although in only one of the German cases was there the characteristic type of radiological appearance described by Caplan (*Thorax*, 1953, **8**, 29).

Among the patients with rheumatoid arthritis a high erythrocyte sedimentation rate was more frequently found in those with advanced silicosis than in the remainder. In 20 cases it was possible to determine accurately the dates of the onset of arthritis and of the first appearance of massive fibrosis, the arthritis developing first in 8, simultaneously with P.M.F. in 5, and subsequently in 7 cases. In only 5 cases was the onset of the two conditions separated by more than 5 years. Although tuberculosis was suspected on radiological grounds in 41 of the 48 cases of P.M.F. with rheumatism, the sputum in every case was negative for tubercle bacilli, so that the author does not agree with Caplan's suggestion that the arthritis may be due to pulmonary tuberculosis. He discusses various mechanisms whereby P.M.F. might predispose to rheumatoid arthritis, but can suggest no acceptable explanation for the undoubted association between the two conditions. *C. M. Fletcher*

1078. **Silico-arthritis.** (Silikoarthritis)
E. W. BAADER. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **13**, 258–266, Oct., 1954. 9 refs.

In reviewing recent work on the association between advanced silicosis and rheumatoid arthritis the author points out that this association was reported almost simultaneously by Caplan in England and Colinet in Belgium, and had been recognized by Petry in Germany [see Abstract 1077] before either of these publications had appeared, while in Brittany the syndrome has been known as the "St. Roch disease" for many years. In place of the various eponymous designations which have been, or may be, applied to this syndrome, the author proposes the term "silico-arthritis". Altogether 178 cases of the syndrome have now been recorded in the literature, but the particular "rheumatoid" type of radiological appearance described by Caplan is rare.

While one case in which tubercle bacilli were eventually found in the sputum is described in detail, active tuberculosis is seldom proved during life in these cases and the

author considers that the arthritis is more likely to be a secondary manifestation of silicosis, although its exact aetiology remains to be determined. *C. M. Fletcher*

1079. **Carcinogenic Studies on Adsorbates of Industrially Polluted Raw and Finished Water Supplies**
W. C. HUEPER and C. C. RUCHHOFT. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **9**, 488–495, June, 1954. 4 figs., 8 refs.

The authors, in an experimental investigation of the possibility of contamination of water supplies by carcinogenic substances, used samples of eluates from carbon filters of four different types of water or effluent, all of which were heavily polluted with oil or industrial waste. These samples, which were analysed chemically, were then applied to the skin of mice.

It was found that the eluate prepared from water containing oil waste possessed some weak carcinogenic properties. There was no evidence of carcinogenic action in the eluates prepared from water polluted by various industrial wastes. The authors point out, however, that since highly concentrated samples were used "it remains at present uncertain whether the observations made have any direct application to population groups consuming water polluted with industrial wastes." *R. E. Lane*

INDUSTRIAL TOXICOLOGY

1080. **Experimental Studies of the Toxicity of Feldspar Dusts.** (Recherches expérimentales sur la nocivité des poussières de feldspath)
A. POLICARD and A. COLLET. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **15**, 343–350, 1954. 4 figs., 6 refs.

In order to compare the toxicity of different forms of feldspar, experiments were carried out at the research laboratories of the Charbonnages de France, Paris–Verneuil, in which rats were given an intraperitoneal injection of 100 mg. of feldspar dust, the particles of which were less than 5 μ in diameter. Three varieties of feldspar were tested—namely, orthoclase, the pericline form of albite, and labradorite. Some of the animals were killed and examined after 1 month and others after 4½ months. Macroscopically there appeared to be little difference in the lesions at the two times of examination. The lymph nodes of the mesentery could be seen to contain small discrete deposits 1 to 3 mm. in diameter, with fine granulations and a hyaline core; most of the nodes were normal in shape but some were enlarged. The lymph channels were swollen with accumulations of phagocytes containing dust particles, which also invaded the lymph nodes, the latter showing an increase in reticular fibres and in collagen.

Of the three types tested, orthoclase, which is the most common of the feldspars and of importance to industry for the manufacture of ceramics and as a source of kaolin, caused the least reaction; after one month the structure of the nodes was unaltered, and after 4½ months it was denser but there was no collagen. Pericline caused a more rapid formation of collagen, and the nuclei of the cells often showed pyknotic changes. The greatest reaction was caused by labradorite, the lesions showing a greenish tinge instead of the more usual white, and fibrosis developing earlier and becoming more intense. The cell nuclei were commonly pyknotic and deformed, and some of the cells contained a very finely divided black pigment.

The authors conclude that the order of toxicity, from the least to the most harmful, among the silicates is as follows: kaolin, mica, orthoclase, pericline, labradorite, fluorspar, and quartz. Some of the changes described are illustrated by photomicrographs.

M. A. Dobbin Crawford

1081. **The Effect of the Intravenous Administration of Sodium Thiosulphate on Blood Lead Content and on the Excretion of Lead in Urine and Faeces in Cases of Lead Poisoning**
D. O. SHIELS, W. C. THOMAS, G. R. PALMER, P. CORNISH, and E. KEARLEY. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 773–782, Nov. 13, 1954. 5 figs., 9 refs.

The beneficial effect of the intravenous administration of sodium thiosulphate in cases of lead poisoning has been amply demonstrated; investigations into the mechanism of this action are described in this paper from the Industrial Hygiene Division of the Melbourne Department of Health.

In the first plan it was found that the administration to 14 patients with lead poisoning of 30 grains (2 g.) of sodium thiosulphate intravenously every second day resulted in a rapid fall in the urinary concentration of lead, as determined by Taylor's turbidometric technique, which was significantly greater than the fall observed in 4 patients not receiving thiosulphate. The concentration of lead in the blood of the former group, however, fell after a temporary initial rise to a greater extent than in the latter. This suggested that the effect of thiosulphate was either to increase elimination of lead in the faeces at the expense of the urine, or to interfere in some way with the precipitation of lead from the urine with calcium oxalate, so that the values obtained by Taylor's method were lower than the real values. In further investigations, therefore, two methods were used in "a considerable number" of urinary lead determinations, the first being a modification of Taylor's technique and the second entailing wet oxidation followed by determination of the lead by a dithizone colour method. With urine from patients not receiving thiosulphate the values obtained by the two methods were the same. But with urine from patients receiving sodium thiosulphate the values obtained by the wet-oxidation technique were significantly (60%) higher than those obtained by Taylor's technique. No explanation for this difference could be found, but it was assumed that values given by the wet-oxidation method, which showed urinary lead excretion to be significantly increased during the first 24 hours after administration of thiosulphate, were the correct ones. Studies of faecal excretion of lead in a few subjects showed that this too was almost certainly increased by giving thiosulphate. *H. B. Stoner*

Forensic Medicine and Toxicology

1082. **Narcoanalysis and Criminal Law**
J. M. MACDONALD. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 283–288, Oct., 1954. 9 refs.

Both lawyers and physicians would object to the use of drugs without the subject's consent in order to obtain a statement from a suspected person, while even when the subject has consented, a statement made while he was under the influence of drugs is legally inadmissible as it has been made involuntarily. Moreover, although such a statement may help the police to obtain other evidence which would lead to the conviction of the suspect, the highly suggestible state induced by such drugs as amylobarbitone may result in misleading answers being given to badly phrased questions, while " the person who is determined to lie will usually be able to continue the deception even under the effects of the drug ". A psychiatrist with experience of narcoanalysis might be more successful than a police officer in obtaining accurate information from a drugged subject, but there are serious ethical objections to his taking part in purely criminal investigations. On the other hand, there appears to be no ethical objection to his carrying out narcoanalysis, provided: (1) that it is part of an examination designed to determine the accused person's state of mind; (2) that his consent has been obtained in writing; (3) that he has been able to consult his lawyer before undergoing the examination; and (4) that any information obtained is not used in evidence at his trial except at the request of the defence. In such circumstances the psychiatrist's attitude to the subject should be friendly, but he must be careful not to use any deception or offer false promises of help.

The main uses of narcoanalysis are to restore speech in those mute, to revive memory in amnesia, and to facilitate the expression of suppressed or repressed thoughts. It may also be used to differentiate between true and false amnesia, material which has been repressed being more likely to be released than that which has been consciously suppressed. But as a means of testing the truthfulness of the subject's statements it is unreliable and should not be used. *G. de M. Rudolf*

1083. **Group-specific Investigations in the Identification of the Victims of an Aeroplane Disaster.** (L'indagine gruppospecifica nella ricomposizione delle vittime di un disastro aereo)
G. FRACHE, A. CARELLA, P. MURINO, and P. FUCCI. *Rivista di medicina aeronautica* [*Riv. Med. aeronaut.*] **17**, 163–177, April–Sept., 1954. 5 figs.

The authors describe investigations undertaken at the Institute of Forensic Medicine of the University of Rome in an attempt to identify the remains of the victims of a disaster at Ciampino Airport, Rome, in which an aircraft exploded on landing, scattering fragments over a radius of 200 to 300 metres. Out of a total of 16 persons (9 crew), it was found possible to distinguish the remains of 11 by serological means, using the following blood-group systems: (1) ABO (with A_1 and A_2); (2) MN; (3) P; and (4) the rhesus groups (C, c, Cw, D, E). What the authors call " the group constellation " afforded a useful means of sorting fragmentary remains for the purpose of reconstruction. This was perhaps helped by the unusual racial diversity of the crew and passengers, who consisted of 7 Filipinos, 4 Anglo-Saxons, 2 Scandinavians, 1 Chinese, 1 Jew, and 1 from the Mediterranean littoral.

The haematological findings, together with the usual clues to identity provided by clothing, papers, tickets, jewellery, and anthropological data (including fingerprints and dentition), served to complete a practical identification of all 16 victims. This is the first time that any extensive use of serological means of identification has been attempted, the amount of blood or tissue fluid available being, as the authors point out, usually too small. In the present study, however, sufficient vascularized tissue remained to provide suitable material for serological identification.

[The remarkable advances in the definition of blood-group characters in recent years have already brought identification by group determination within sight. Race and Sanger recently found that of 132 members of the Lister Institute, London, no less than 126 could be distinguished from their colleagues by their blood-group complex. The use of this method in identifying the victims of air disasters has not, however, previously been explored—its application must always be subject to the restrictions imposed by lack of knowledge of the blood groups of passengers, if not of flying personnel—and this article makes a most useful contribution to the development of procedures for the identification of the scattered parts of disintegrated victims and the apportioning of their remains.] *Keith Simpson*

1084. **The Histological Characteristics of Post-mortem Burns.** (Les particularités histologiques des brûlures " post mortem ")
O. JANEZIC-JELACIC. *Annales de médecine légale et de criminologie* [*Ann. Méd. lég.*] **34**, 63–71, March–May, 1954. 3 figs., 8 refs.

To determine whether death is the result of murder, suicide, accident, or natural causes it is necessary in some cases to establish whether burns found on the body originated during life or after death. The author describes a case in which second-degree burns containing fibrin and even leucocytes were found on the body of a victim of an air crash, although the injuries due to impact must have been immediately fatal and the plane did not catch fire until after it struck the ground. She claims that in this case inflammatory changes must have been produced in the skin after death, and concludes that when it is important to establish whether burning preceded or followed death, the fact must be accepted

that for 10 to 20 minutes after the death of a subject the skin can produce an inflammatory reaction with leucocytic infiltration, since molecular life still exists in it, and that the dividing line between ante-mortem and post-mortem phenomena is not precise, certainly so far as the skin is concerned.

The author has studied the histological aspects of the problem at the Army School of Medicine, Belgrade, and describes a curious state of the epidermis which is found in post-mortem burns of the skin. The stratum corneum remains normal, but the other layers become indistinct. Between the basal and cornified layers there are bundles of long, narrow cells resembling fibroblasts, with almost linear nuclei, these bundles being disposed sometimes vertically, sometimes at an angle or almost horizontally. If the action of the heat is prolonged, post-mortem vesicles are formed, raising the epidermis. Both in burns produced experimentally in various ways on the bodies of 36 subjects and in specimens from cases of accidental post-mortem burning the histological picture described above was consistently found, and not that usually accepted as being characteristic of post-mortem burns. Moreover, identical appearances are seen in the skin in certain cases of electrocution, the author postulating that this is due to the high temperature generated by the continued passage of the electric current after the skin has been killed. *Gilbert Forbes*

1085. **Poisoning by Cantharidin**

L. C. NICKOLLS and D. TEARE. *British Medical Journal* [*Brit. med. J.*] **2**, 1384–1386, Dec. 11, 1954. 4 figs., 14 refs.

In this paper, from the Metropolitan Police Laboratory, New Scotland Yard, and St. George's and St. Bartholomew's Hospitals, London, 2 fatal cases of cantharidin poisoning are described. The history and properties of cantharidin are briefly reviewed, with special reference to methods for identification of the compound. The authors found that only three tests were reliable: (1) melting point; (2) production of characteristic pain and blistering when the substance was applied to the skin of the arm; and (3) *x*-ray diffraction pattern of the crystalline material. The clinical history in the 2 cases was similar. Two female clerks, aged 19 and 27, ate some coconut ice offered to them by a male employee working in the same firm of chemists. A few minutes later both the women felt ill and vomited, and later the same day one was admitted to hospital with a diagnosis of haematemesis. After washing out the stomach and administration of morphine her condition improved, but she later vomited about half a pint (250 ml.) of fresh blood, collapsed, and died 16½ hours after eating the coconut ice. The other patient died about 26 hours after eating the confection. [The clinical features in the latter case are described in Abstract 1086.]

Post-mortem examination revealed an almost identical picture in both cases: destruction of the mucosa of the mouth and oesophagus, intense engorgement of the whole of the genito-urinary tract, with frank blood in the renal pelves, ureters, bladder, and ovaries, haemorrhage in the heart and lungs with, in the first case, severe pulmonary oedema and early fatty change in the liver. The male employee was himself admitted to hospital with blisters on the face but no signs of general poisoning. In the office of the employees some minute crystals were recovered from the surface of a desk and material was taken from the tips of a pair of scissors. Using the *x*-ray diffraction method the authors found that the former were cantharidin crystals and the latter was a mixture of cantharidin and coconut ice. Crystalline cantharidin was recovered from vomitus, but only an amorphous product could be obtained from extracts of the organs. Varying proportions of the residue were tested under uniform conditions by the skin-blister method, and it was concluded that 65 to 130 mg. of cantharidin was circulating in the organs. [For details of the methods of estimation the original paper should be consulted.] The male employee later pleaded guilty to a charge of manslaughter of both the girls. *P. N. Magee*

1086. **Cantharidin Poisoning**

J. D. CRAVEN and A. POLAK. *British Medical Journal* [*Brit. med. J.*] **2**, 1386–1388, Dec. 11, 1954. 12 refs.

The clinical features in a fatal case of cantharidin poisoning, seen at University College Hospital, London, are described. [For the post-mortem findings and other details see Abstract 1085.] The patient, a female aged 19, complained of abdominal pain and nausea some 10 minutes after eating coconut ice; the pain became worse after taking sodium bicarbonate and was accompanied by an intolerable burning sensation in the mouth and throat. On admission 2½ hours later she was vomiting blood-stained mucus and had diarrhoea which contained no frank blood. Her general condition was poor and she was in great pain. A small blister was noted at the left angle of her mouth, and the tongue was swollen, with peeling epithelium which extended to the fauces and soft palate. There was generalized abdominal tenderness, without rigidity, but no tenderness in the loins. No evidence of abnormality in the heart or lungs was found, but there was tenderness over the trachea at the root of the neck. The skin showed no erythema, blistering, or petechiae. The patient was given 0·25 gr. (16 mg.) of morphine and an intravenous infusion of 5% dextrose in normal saline. No attempt was made to pass a stomach tube because of the excoriation of the mouth and fauces. The patient's general condition remained unchanged until 14 hours after the poison had been taken, when it rapidly deteriorated. No urine was passed spontaneously and a catheter specimen, 16 hours after ingestion, contained some deeply blood-stained urine. With the onset of collapse intravenous infusion of dextran was started, and the patient was given dimercaprol intramuscularly and niketha mide intravenously, but no improvement occurred and it became necessary to pass a tracheal tube. The blood pressure continued to fall in spite of intravenous administration of noradrenaline (80 μg. per minute), and the patient died about 26 hours after taking the cantharidin. Investigations showed increasing haemoglobin concentration in the blood, with no spectroscopic evidence of acute haemolysis. The blood picture was characteristic of bone-marrow stimula-

tion. The *p*H of vomited mucus was found to be approximately 9.

A preliminary diagnosis of severe irritant poisoning was made, and the *p*H of the vomitus at first suggested " the remote possibility " of poisoning from caustic soda. Later, however, cantharadin was suspected, and this became more probable when oliguria and haematuria were discovered. It was then learned that the post-mortem findings in the other case were characteristic of cantharidin poisoning.

The authors discuss the blood picture, concluding that it is probably peculiar to cantharidin among the irritant poisons, and compare it to the leuco-erythroblastic response seen in mustard-gas poisoning. They also comment on the absence of pain in the loins. No specific treatment is known, and it is suggested that since preparations of cantharidin have no special virtue and are highly dangerous they should no longer be made available for therapeutic purposes. *P. N. Magee*

1087. **A Case of Cantharidin Poisoning**
M. A. LÉCUTIER. *British Medical Journal* [*Brit. med. J.*] **2**, 1399–1400, Dec. 11, 1954. 4 refs.

A man, aged 43, a keen fisherman, used cantharidin, which he obtained from an illicit source, to mix with bait for attracting fish. He stated that during his preparations he used his thumb to occlude the opening of the bottle containing the mixture, subsequently pricked the thumb with a fish-hook, and then immediately sucked it. Approximately half an hour after ingestion he felt ill and began to vomit; shortly afterwards diarrhoea started. Vomiting and diarrhoea continued for 2 days and then ceased, but the following day his condition was worse and he was admitted to the Royal Hospital, Chesterfield, with a complaint of abdominal and back pains. There had been some haematuria but very little urine had been passed since the day before admission. On examination the patient was found to be severely shocked, with slight generalized abdominal tenderness and weakness of the arm and leg muscles. In spite of the usual resuscitative measures his condition gradually deteriorated and he died 6 hours after admission. The blood urea level was 160 mg. per 100 ml. and there was evidence of haemoconcentration (haemoglobin 19·2 g. per 100 ml.; erythrocytes 6,500,000 per c.mm.).

At necropsy no sign of irritation of the mouth or oesophagus was found, but the stomach was moderately injected, with some petechiae in the pyloric antrum. There was marked injection of the whole of the duodenal mucosa with moderate injection of the first 12 in. (30 cm.) of the jejunum and of all the terminal ileum; there was, however, no mucosal ulceration. The kidneys appeared normal macroscopically but the bladder contained a small volume of heavily blood-stained urine. Microscopically, the kidneys showed acute tubular necrosis. The stomach contents, liver, kidney, and bladder urine were all analysed for various irritants, including cantharidin, but the results were entirely negative. No pathogenic organisms were found in the contents of the small intestine. The author comments on the absence of lesions in the upper alimentary tract, which he believes to be due to the insolubility of the alkaloid, which was quickly swallowed in the saliva. He suggests that the failure to find the poison in the organs and body fluids can be explained by excretion of the alkaloid during the 3-day period between ingestion and death and by the relative insensitivity of the skin-blister test in the circumstances in which this was performed, the material available having to be divided into several fractions for the purpose of testing for other irritants. *P. N. Magee*

1088. **A Rapid Method for the Estimation of Morphine**
J. M. FUJIMOTO, E. L. WAY, and C. H. HINE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*) **44**, 627–635, Oct., 1954. 3 figs., 12 refs.

A rapid extraction method for the photometric estimation of morphine in biologic media is described. The method utilizes single extraction techniques and has a high degree of specificity for morphine. Considerable time-saving is accomplished by extracting morphine from a highly alkalinized solution with *n*-butanol to give the major separation of the morphine from the extraneous interfering material. Subsequent extraction steps remove further interfering substances without undue loss in time or yield of morphine. A colorimetric phenol reagent is used for the final estimation of the morphine in the buffer extract. A highly specific test for morphine is also obtained by simply incorporating the ultraviolet absorption and partition ratio determinations into the general procedure. Two actual cases of morphine poisoning were established by the use of the developed method.—[Authors' summary.]

1089. **Use of Artificial Kidney for Removal of Barbiturates in Dogs**
I. SUNSHINE and J. R. LEONARDS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 638–641, Aug.–Sept., 1954. 14 refs.

Experiments were conducted at Cleveland, Ohio, to determine whether haemodialysis was of value in the treatment of barbiturate poisoning. A number of dogs were given a known dose of various barbiturates, some animals being left untreated while the blood of others was subjected to dialysis in an artificial kidney of the Skegg–Leonards type, starting 1 to 3 hours after the dose. The dialysing fluid was of the same electrolyte composition as the extracellular fluid of dogs, and 200 to 300 litres was used in 4 to 8 hours.

With sodium pentobarbitone 3 out of 8 control animals and 2 out of 7 treated dogs died. With amylobarbitone one out of 5 controls and none of the treated dogs died. With a large dose of phenobarbitone 4 of 5 controls died, whereas all 6 treated animals survived. In each case the plasma barbiturate level fell more rapidly with dialysis than without.

It is concluded that haemodialysis may be of value in the treatment of severe poisoning with a long-acting barbiturate such as phenobarbitone, but is unlikely to be helpful in the case of short-acting barbiturates. It is emphasized that the rate of dialysis is slow and that treatment should be continued longer than is usual in cases of renal insufficiency. *G. Loewi*

Anaesthetics

1090. Hypothermia. Part I. A Technique of Blood Stream Cooling. Part 2. Physiological Observations during Hypothermia

D. N. Ross. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **103**, 97–138, 1954. 25 figs., bibliography.

A technique for the production of hypothermia and its use to enable a dry operative field to be provided within the heart during experimental cardiac surgery in dogs are described in the first part of this paper from Guy's Hospital, London. Blood was conducted from the femoral artery to the femoral vein through a coil of siliconized polythene or "portex" tubing immersed in brine cooled by a refrigerator to −5° C. No anticoagulant was necessary. An hour after premedication with morphine, 10 mg., and atropine, 0·6 mg., anaesthesia was induced and maintained with intermittent thiopentone and ether. A cuffed tube was passed into the trachea and connected to a source of 100% oxygen, soda-lime absorber, and rebreathing bag. During the cooling process anaesthesia was just deep enough to prevent shivering, while at temperatures below 28° C. no further anaesthetic was necessary. The temperature fell by 1° C. every 5 minutes, reaching 25° C. in 1 hour. Cooling was then stopped by clamping the artery and removing the apparatus. With exposure to room temperature hypothermia was maintained for an hour or more, giving ample time for surgery.

During cooling the pulse rate was found to bear a linear relationship to temperature. The blood pressure was maintained at first, and then fell slowly to reach 70 to 80 mm. Hg at 25° C. The respiration rate first increased, but below 35° C. both rate and depth diminished and breathing was barely perceptible at 28° C. When respiration became inadequate, ventilation by compression of the rebreathing bag was instituted to avoid anoxia and cyanosis. After the operation, the animal was covered to prevent shivering and allowed to rewarm spontaneously. Various operative procedures on the heart and great veins were carried out and are described, together with a technique devised to maintain the coronary flow after clamping the ascending aorta and pulmonary trunk, whereby blood from the inferior vena cava was pumped into the arterial system via the femoral artery. In this way strong ventricular contraction could be maintained for 15 to 20 minutes after clamping the aorta, and coronary air embolism during open heart surgery was prevented.

Certain physiological observations during hypothermia are described in the second part of the paper. The clotting time at normal body temperature was 4 minutes, and at 25° C. 12 to 15 minutes. Urinary secretion diminished with cooling and ceased at about 25° C., as judged from catheter specimens taken at ½-hourly intervals during cooling. Very rapid cooling markedly reduced the cardiac output and increased the tendency to ventricular fibrillation. Oxygen consumption at 25° C. was 39% of normal, and at 20° C. it was 25% of normal. The oxygen content of the blood, both arterial and venous, increased by 2 volumes % at 25° C. owing to increased solubility, while the arterio-venous oxygen difference remained normal. Both cardiac output and blood pressure were lowest during the early stages of rewarming, and the risk of death was greater then than at other times. The electrocardiogram showed slurring and notching of the downstroke of the R wave, and flattening of T progressing to inversion, sometimes followed by ventricular fibrillation on stimulation. Haematocrit values showed a 10% increase during spontaneous respiration and 3·6% increase with hyperventilation at 25° C. The *p*H of the blood during spontaneous respiration was 7·0 to 7·1 at 25° C. with a rising plasma carbon dioxide content, while with vigorous hyperventilation it rose in some cases above 7·6, with a correspondingly reduced plasma carbon dioxide content. In the former case ventricular fibrillation was liable to develop on stimulation, in the latter cardiac arrest in asystole.

B. L. Finer

1091. A Simple Method for Inducing Hypothermia

B. Blades and H. C. Pierpont. *Annals of Surgery* [*Ann. Surg.*] **140**, 557–562, Oct., 1954. 4 figs., 11 refs.

The present status of intracardiac surgery may be compared with that of thoracic surgery before effective control of intrapleural and intrapulmonary pressure was made possible by anaesthetic techniques. Most intracardiac manipulations are tactile; exposure is inadequate. Protection of the brain during exclusion of the heart from the circulation is the chief problem, and until an adequate heart pump is available hypothermia may be helpful. In the present paper from the George Washington University School of Medicine, Washington, D.C., a safe and simple method of producing hypothermia is described.

It has been shown that the brain of a deeply cooled animal can survive 15 to 20 minutes without the heart, compared with 3 to 5 minutes when the temperature is normal. In the human subject hypothermia can be dangerous, despite lowered tissue oxygen demands, because of the risk of ventricular fibrillation. The latter may result from tissue anoxia regardless of the amount of oxygen in the circulating blood—in other words, anoxia without anoxaemia. Heart-tissue anoxia can be detected in the electrocardiogram before irreversible changes have occurred, being shown by inversion of the T wave and prolongation of the conduction time. A technique for inducing hypothermia which can be reversed quickly is therefore desirable. The authors describe a method of intrapleural cooling, which is more rapid than, and has not the disadvantages of, skin cooling and can be discontinued or reversed easily. Cold saline solution is allowed to bathe the bed of the lung, the aorta, and the

pleura, the overflow being siphoned off. The solution is in contact with a large surface, and therefore cools a major portion of the circulating blood. This technique was used in one case, that of a man with an aneurysm of the aortic arch. During the cooling, changes in the electrocardiogram indicated myocardial anoxia on nine different occasions. The flow of the cold saline solution was discontinued temporarily and the inverted T wave returned to normal after nine or ten beats of the heart, when cooling was resumed. The body temperature was lowered to 30° C. in 2 hours 35 minutes; rewarming required 1 hour 55 minutes. The aortic arch was clamped and aneurysmorrhaphy was performed in 18 minutes. The patient made an uneventful recovery.

W. Stanley Sykes

1092. **Some Physiologic Concepts of Hypothermia and Their Applications to Cardiac Surgery**

W. G. Bigelow, W. T. Mustard, and J. G. Evans. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 463–480, Nov., 1954. 7 figs., 24 refs.

In view of the increased interest in hypothermia the authors, writing from the University of Toronto, review the physiological changes which occur in this procedure and consider its application to cardiac surgery.

The lowering of body temperature to 20° C. (68° F.) reduces oxygen consumption, provided there is no shivering, to about 15% of normal. Blood pressure, heart rate, and cardiac output are all lowered by cooling; the venous pressure rises slightly, and rises still further if prolonged, vigorous, positive-pressure respiration is carried out. The electrocardiogram and electroencephalogram show typical changes. Animals appear to tolerate cooling better if the *p*H of the plasma is higher than normal; hyperventilation causes a reduction in the serum potassium level. Ventricular fibrillation may occur if the temperature is reduced too much. In monkeys kept at 16° to 19° C. (61° to 66° F.), the circulation could be interrupted for 24 minutes, with survival in 12 out of 13 animals. Young animals are more tolerant of cold than adults, and a 10-week-old puppy survived after being cooled to 10° C. (50° F.). A study of natural hibernation showed that the groundhog hibernates at 3° C. (37° F.), and can be cooled to this temperature by means of anaesthetics; of 6 groundhogs kept at 3° C., 5 survived after interruption of the circulation for 1 to 2 hours. It has been suggested that a "hibernating gland" which is widely distributed throughout the body is responsible for this tolerance to cold and attempts have been made to extract the active principle.

The authors have been conservative in the use of hypothermia for the performance of intracardiac operations in human subjects, but have used it as an adjunct to surgery in poor-risk patients, particularly in cases of mitral valvotomy. Various methods have been described. The authors' method is to give promethazine, chlorpromazine, and pethidine, 50 to 100 mg. of each, intravenously for one hour before cooling with a refrigerating blanket is instituted, administration being continued during cooling. At about 34° C. (93° F.) anaesthesia is induced with a small dose of thiopentone, and further shivering is controlled with thiopentone or ether; intubation is performed and hyperventilation employed. Children are intubated before cooling is begun. Rewarming is carried out by means of hot water bottles up to 33° C. (91° F.), and the patients are then allowed to return to normal temperature spontaneously; the temperature should not be allowed to fall below 28° C. (83° F.), at which level the circulation may be interrupted for 6 to 8 minutes. If the temperature has fallen below 28° C. rewarming to 33° C. should be carried out as rapidly as possible either by immersion in warm water or by diathermy.

D. D. C. Howat

1093. **Hypothermia with Autonomic Block for the Poor Risk Patient in Thoracic Surgery**

R. S. Barclay, K. C. Grigor, J. G. Stevenson, and T. M. Welsh. *Glasgow Medical Journal* [*Glasg. med. J.*] 35, 235–243, Oct., 1954. 4 refs.

The authors describe the methods of hypothermia with autonomic block adopted at Mearnskirk Hospital, Newton Mearns, Renfrewshire, in operating on 3 cases of far-advanced pulmonary tuberculosis and 2 of bronchial carcinoma with abscess formation which were considered unfit for pneumonectomy with the usual anaesthetic methods. Premedication was with promethazine (50 mg.) and pethidine (50 to 100 mg.) given orally or intramuscularly 4 hours before operation. A 5% glucose drip was then started, and 1 ml. of "lytic cocktail" (pethidine 100 mg., promethazine 50 mg., and chlorpromazine 50 mg.) injected as a test dose; this usually caused somnolence, and if no excessive narcosis or marked fall in blood pressure occurred a further 1 to 2 ml. was injected at 10- to 15-minute intervals until deep narcosis was obtained, with slow respiration and pulse rate and usually improved colour. At 60 to 90 minutes after the start of the infusion the patient was covered with a cold, wet sheet, and if there was no shivering ice-bags were placed in the axillae and groins; slight shivering was controlled with thiopentone. When the rectal temperature (measured by a thermistor) fell to 33° or 34° C. active cooling was discontinued, as a further fall of 1° to 3° C. usually takes place during the operation. Anaesthesia was induced with thiopentone and maintained with nitrous oxide and oxygen with controlled respiration, using tubocurarine as relaxant. Meticulous care was taken to protect pressure points, and blood lost was replaced by transfusion.

Pulse rate and blood pressure were lower than usual, and haemorrhage was reduced; it was also clear that shock-producing stimuli had much less effect, although cardiac irregularities were not abolished. The face-down position was used, without blocking the bronchus. Rewarming was gradual, and normal temperature was not regained for up to 72 hours. Pethidine in doses of 50 mg. readily controlled postoperative pain, which was less than usual. Transient pulmonary oedema occurred in 2 cases, and the authors stress that the administration of intravenous fluids must be carefully controlled. One patient died of recurrence of carcinoma in the bronchial stump, but the other 4

recovered, in spite of their poor condition. Although doubtful of the general use of hypothermia in thoracic surgery, the authors feel that in cases like those described this technique may make operation possible.

D. D. C. Howat

1094. **The " Lytic Cocktail ". Observations on Surgical Patients**

R. SHACKMAN, F. G. WOOD-SMITH, I. G. GRABER, D. G. MELROSE, and R. B. LYNN. *Lancet* [*Lancet*] **2**, 617–620, Sept. 25, 1954. 4 figs., 17 refs.

At Hammersmith Hospital (Postgraduate Medical School of London) a series of 17 patients, most of them male, received the " lytic cocktail ", as described by Laborit and Huguenard (*Presse méd.*, 1951, **59**, 1329), as part of the premedication for major urological operations, and observations were made on the circulation, temperature, and oxygen consumption. After an oral dose of 50 mg. of promethazine the night before and 100 mg. of pethidine and 50 mg. of promethazine intramuscularly 2 to 3 hours before operation the right auricle was catheterized to facilitate the estimation of the oxygen content of mixed venous blood; oxygen uptake was measured by means of a spirometer, and peripheral pulse volume by means of a digital plethysmograph. Observations were then made before and after the intravenous infusion of the " cocktail ", consisting of pethidine (100 mg.), promethazine (50 mg.), and chlorpromazine (100 mg.) in normal saline. When the " cocktail " had achieved its maximum effect nitrous oxide and oxygen were given endotracheally and thiopentone and gallamine triethiodide intravenously as required to maintain adequate anaesthesia and relaxation for surgery. The patients were clad in normal theatre garb, and no artificial cooling was used.

The conclusions reached were that, in the unexposed patient, the " cocktail " produces no fall in temperature or oxygen consumption but, in spite of a fall in blood pressure, there is a rise in cardiac output associated with the reduction in systemic resistance. The dilatation of superficial veins facilitates the rapid administration of intravenous infusions, but it is doubtful whether these circulatory effects differ from those produced by other vasodilator drugs.

Donald V. Bateman

1095. **The Change in Pulmonary Alveolar Ventilation Achieved by Aiding the Deflation Phase of Respiration during Anesthesia for Surgical Operations**

F. F. ALLBRITTEN, G. J. HAUPT, and J. H. AMADEO. *Annals of Surgery* [*Ann. Surg.*] **140**, 569–582, Oct., 1954. 5 figs., 28 refs.

Spontaneous respiration during anaesthesia is often insufficient to maintain normal levels of oxygen or carbon dioxide in the blood, even with a patent airway. This may be due to the use of depressant or paralytic drugs, the anaesthetic, the position of the patient, or the nature of the operation. Oxygen lack may be recognized by a change in the patient's colour, but there is no clinical evidence of carbon dioxide retention. Thus the absence of cyanosis gives no proof that pulmonary ventilation is adequate. Carbon dioxide retention frequently occurs, but its detection is complicated and time-consuming. Respiratory acidosis can be prevented by manual compression of the breathing bag, but this method has certain disadvantages. Even if inflation is efficient, deflation is left to the natural contractility of the lung.

In this paper from the Jefferson Medical College Hospital, Philadelphia, an apparatus to assist deflation with a slight intratracheal vacuum is described; it is attached to the standard anaesthetic apparatus. A 5-litre rebreathing bag is housed in a sealed chamber with one side replaced by bellows driven by a motor of the type commonly used in a windscreen-wiper. A large opening between the bellows and the chamber permits large volume changes at low pressure, which can be regulated from 12 cm. to −6 cm. of water.

The apparatus was used on 6 patients undergoing pneumonectomy and 17 subjected to other open-thorax operations, these procedures providing the most severe tests of methods of ventilation. In all cases the machine took over the respiratory rhythm from the patient without the aid of paralytic drugs, and the conditions for operation were good. In no instance did respiratory acidosis occur.

The authors consider it possible that cardiac irregularities during and following operation are related to carbon dioxide retention.

W. Stanley Sykes

1096. **Pentolinium Tartrate in Controlled Hypotension**

G. E. H. ENDERBY. *Lancet* [*Lancet*] **2**, 1097–1098, Nov. 27, 1954. 14 refs.

The author reports his experience at the Queen Victoria Hospital, East Grinstead, Sussex, with the new autonomic ganglion blocking agent pentolinium tartrate (" ansolysen ")—which is stable in aqueous solution, can be autoclaved, and contains 44·5% of the active pentolinium cation—in the induction of controlled hypotension in 180 patients aged from 5 to 78 years. There were no undesirable side-effects. The procedure is as follows. After induction of anaesthesia the blood pressure is taken and then 15 to 20 mg. of ansolysen is given intravenously to the normotensive patient in the horizontal position 3 to 5 minutes before operation. After 3 minutes the effect on the blood pressure is assessed before tilting. The table is then lowered into the reversed Trendelenburg position until a practical and safe level of blood pressure (often 60 to 70 mm. Hg), as measured at heart level on the arm, is achieved. In hypertensive patients half the above dose is used, and for those over 50 the dose is reduced by 5 to 10 mg., even if blood pressure is normal.

The author lists the advantages of pentolinium tartrate over other hypotensive agents as follows. (1) The drug causes a slow initial fall in blood pressure, and there is no undue hypotension in the horizontal position. (2) Change of posture and controlled or assisted respiration have more hypotensive effect. (3) In hypertensive patients profound hypotension occurs slowly and without ill effect. (4) Hypotension can be maintained longer and often at a lower level, with a slow return to normal. (5) When a small initial dose is given to a hypertensive patient tolerance is slow and further doses increase the hypotension in most cases, but with a large initial dose

in young patients tolerance is rapid, and further doses are ineffective. In such cases procainamide and hexamethonium bromide may be given with advantage. (6) Tachycardia is rare and soon disappears. (7) The relaxant effects of decamethonium are not reversed by the drug as they are by hexamethonium. The main disadvantage of pentolinium tartrate is that, in combination with chlorpromazine, tachycardia frequently occurs and the hypotension is then poor. With the addition of "arfonad", however, tachycardia still occurs but hypotension is satisfactory. *B. L. Finer*

1097. A Study of Liver Damage following Induced Hypotension

W. G. ANLYAN, W. W. SHINGLETON, W. R. BENSON, C. R. STEPHEN, M. SALEM, and H. M. TAYLOR. *Surgery* [*Surgery*] **36**, 375–383, Sept., 1954. 3 figs., 23 refs.

Marked changes in the gross appearance and function of the liver have been reported to occur during hypotensive anaesthesia, and this paper from Duke University School of Medicine, Durham, North Carolina, describes an attempt to evaluate biochemically the extent of the damage caused to the liver by this procedure in 41 dogs. Before, and twice weekly after, a period of controlled hypotension the blood non-protein nitrogen and serum bilirubin, chloride, sodium, and potassium levels were determined, the carbon dioxide combining power of the blood estimated, and the "bromsulphalein" retention and thymol turbidity and flocculation tests were performed. The animals were anaesthetized with intravenous pentobarbitone sodium, and 100% oxygen was given through an endotracheal tube with non-return valve, respiration being assisted or controlled as necessary. The blood pressure was reduced to 30 mm. Hg, which is equivalent to the abolition of peripheral arteriolar resistance, either by an intravenous drip infusion of "arfonad", a ganglion-blocking drug, or by bleeding. Arfonad was given to 10 dogs for 30 minutes and to 11 for 45 minutes, after which the blood pressure rose gradually to normal, assisted in some cases by the administration of vasopressor drugs. For comparison, 20 dogs were bled through a polythene catheter inserted in the inferior vena cava until the desired blood pressure was reached, the level then being maintained by occasional withdrawals for 30 minutes in 10 cases and 45 minutes in the other 10, the blood being returned to the dog afterwards. At the beginning of the period of hypotension 20,000 units of aqueous penicillin and 300,000 units of procaine penicillin were given, followed by 300,000 units of procaine penicillin daily for one week. The dogs were killed after 15 to 30 days and the viscera examined.

The mortality was higher after haemorrhagic hypotension than after chemically induced hypotension. Prolongation of the hypotensive state increased the mortality. Among the survivors biochemical evidence of liver damage appeared between the 3rd and 21st days but in all except one case was transient. There was relatively little difference between the two groups in the incidence or severity of the damage.

Significant histological changes in the liver were found only in animals dying within 2 days of the period of hypotension. Where death had occurred within 24 hours there were necrosis of the paracentral cells and dilatation of the paracentral sinuses. Where death occurred within 24 to 48 hours, parenchymatous necrosis was more obvious and extensive and the paracentral cells contained numerous small sudanophilic globules; these were non-specific but suggestive of the effects of anoxia. None of the other organs examined, which included the heart, lungs, kidneys, and adrenal glands, showed significant changes. It is suggested that, apart from the brain, the liver is the organ most sensitive to the hypoxia of induced hypotension. *B. L. Finer*

1098. Cardiac Arrest during Anesthesia and Surgery. An Analysis of 30 Cases

J. P. WEST. *Annals of Surgery* [*Ann. Surg.*] **140**, 623–629, Oct., 1954. 1 fig., 12 refs.

In the author's view cardiac arrest should be preventable in good-risk patients. Hypoxia, vagal reflexes, hypercapnia, and toxicity or overdose of anaesthetic agents are some of the factors thought to be responsible for sudden cardiac arrest. Further, the high incidence of cardiac arrest in congenital cyanotic heart disease (1 in 18) suggests that a decrease in oxygen saturation is an important aetiological factor. It is emphasized that the part played by the individual anaesthetic agent is difficult to assess, since it is common practice for several drugs to be used for premedication and for induction and maintenance of anaesthesia.

Between 1947 and 1953 at St. Luke's Hospital, New York, fatal cardiac arrest occurred in 30 out of 35,000 patients subjected to anaesthesia for operation. A disproportionate number of deaths (7) occurred in children under 10 who had not received any preoperative medication. Of the 23 adults, 14 were considered to be reasonable operative risks while 9 were considered to be poor risks for anaesthesia and operation; nearly all received premedication, and in 16 cases thiopentone was one of the anaesthetic agents. There was evidence of hypoxia in 19 of the 30 patients, in that they were cyanotic before heart failure set in. In 8 patients the heart failed during induction, in 11 during operation, and in 11 at the end of or just after the operation.

Measures taken to reduce the risk included: (1) adequate oxygenation throughout anaesthesia; (2) discontinuance of thiopentone in many cases; and (3) the use of atropine or hyoscine preoperatively in children. When these measures were adopted the incidence of cardiac arrest fell from 1 in 1,000 to 1 in 2,200 cases.

W. Stanley Sykes

1099. Thiopentone as a Factor in the Production of Liver Dysfunction

J. W. DUNDEE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 14–23, Jan., 1955. 2 figs., 35 refs.

1100. A Study of Anesthesia for 1,176 Transurethral Prostatectomies

C. L. GRAVES, F. M. SELLERS, and M. KARP. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1045–1048, Nov. 13, 1954. 3 refs.

Radiology

RADIOTHERAPY

1101. Epithelioma of the Buccal Mucosa

J. E. BREED. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 72, 806–812, Nov., 1954. 2 figs., 3 refs.

The author describes the method adopted at the Breed Radium Institute, Chicago, for the treatment of epithelioma of the buccal mucosa in 51 patients between 1930 and 1949. In such cases, after careful physical examination of the growth, internal and external radon applicators are used concurrently. The internal applicator measures 1·5×2 cm., contains 400 to 800 mc. of radon, and has an active surface area of 1·5 sq. cm. Screening is by 2 mm. of silver, 1 mm. surrounding the glass radon tube and 1 mm. in the silver box carrying the tubes, and the box is surrounded by 4 mm. of rubber. The applicator is held by hand against the tumour by means of a long rod, the operator standing behind a lead plate 2½ inches (6·5 cm.) thick, and is placed successively for 5 minutes against enough points around the tumour to produce the effect of a circular applicator with the radon at the periphery. For tumours less than 2 cm. in diameter, 4 points suffice; for larger tumours 2 points are treated daily. The external applicator is 4 cm. square, contains 500 mc. of radon, and is applied at a distance of 2 to 4 cm. from the skin surface external to the tumour. Treatment is spread over 3 or 4 weeks and the total dose in the author's series ranged from 5,000 to 8,000 r, 80% of this being given from the mucosal surface and 20% from the skin. When bone was involved irradiation was followed by radical surgery. Metastases in lymph nodes were treated by teleradium concurrently, and if still present when the primary tumour had been controlled were removed, if operable, by block dissection.

The author's 51 cases were divided into 20 favourable cases (that is, cases of short duration and without bone involvement or metastasis), with 80% recovery (16 cases), and 31 unfavourable cases (of longer duration and with metastatic involvement), with only 9% recovery (3 cases). For the entire series the 3- and 5-year cure rates were 37·2% and 35·7% respectively. *G. E. Flatman*

1102. Massive Preoperative Irradiation in the Treatment of Osteogenic Sarcoma in Children. A Preliminary Report

K. C. FRANCIS, R. PHILLIPS, J. J. NICKSON, H. Q. WOODARD, N. L. HIGINBOTHAM, and B. L. COLEY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medecine* [*Amer. J. Roentgenol.*] 72, 813–818, Nov., 1954. 10 refs.

It has been suggested that heavy preoperative irradiation followed by amputation offers the best hope for patients with osteogenic sarcoma. During a period of 2 years (1951–2), therefore, at the Memorial Center for Cancer and Allied Diseases, New York, 15 patients (10 females and 5 males) aged between 7 and 17 with osteogenic sarcoma were treated by irradiation with doses of 1-meV *x* rays ranging from 6,000 to 12,000 r given over 5 to 10 days; other factors were: 3 mA, filter of 7 mm. wolfram, 2 mm. Hg, and 8 mm. Cu, and H.V.L. of 3·8 mm. Pb. Two fields were used, either anterior and posterior or medial and lateral, and they varied in size from 15×7 cm. to 26×17 cm. Amputation followed within 3 days of completion of irradiation, incision through irradiated skin being meticulously avoided. For the 7 femoral tumours high thigh amputation was performed in 5 cases and disarticulation at the hip-joint in 2 cases; low thigh amputation was carried out for the 8 tibial tumours. It is stressed that the tumour frequently spreads proximally through the marrow cavity and therefore examination of marrow-biopsy smears for malignant cells at the time of amputation is recommended so that immediate disarticulation at the hip-joint can be performed if necessary.

In the cases discussed the duration of symptoms before admission ranged from 2 weeks to 9 months. A biopsy specimen of the tumour was obtained by aspiration or open operation in all cases. In no case had metastases occurred before treatment, but these appeared in 10 patients within 3 to 22 months after amputation. The serum and tumour phosphatase levels were studied, but were found not to be increased in 7 of the cases. In one, however, the initial serum phosphatase level was high (55·7 units per 100 ml.), increased to 73·4 units per 100 ml. during irradiation, and fell to the upper limit of normal one week after amputation. Systemic and local effects of the massive irradiation were surprisingly slight, erythema being noted in 8 patients, nausea in 2, and leucopenia in one.

Ten of the patients have been observed for one year or more; of these, 3 are alive with no disease, 2 are living but have metastases, and 5 are dead. The remaining 5 patients were treated more recently, and so far all are well with no sign of disease 2 to 7 months after operation. The authors do not consider that these results are very encouraging or that this method of treatment increases the survival rate, but refrain from drawing definite conclusions in view of the small numbers and the short period of observation. *G. E. Flatman*

1103. Alkoxyglycerols in the Treatment of Leukopenia Caused by Irradiation

A. BROHULT and J. HOLMBERG. *Nature* [*Nature (Lond.)*] 174, 1102–1103, Dec. 11, 1954. 4 refs.

Certain α-alkoxyglycerol esters, which are normally found in the bone marrow and other haematopoietic organs, have been used in the treatment of radiation leucopenia in 36 patients undergoing radiotherapy at

Radiumhemmet, Stockholm. The esters were administered by mouth, and in 25 cases there was an immediate increase in the leucocyte count; in only 2 cases was there further deterioration. A striking example of the benefit obtained is given in the case of a nurse employed in radium therapy whose leucocyte count had been about 2,000 per c.mm. for more than a year. After 4 days' treatment with alkoxyglycerols the figure had risen to 3,600 per c.mm. and remained at this level for 5 months, when a further course of treatment raised it to 4,200 per c.mm.

The use of alkoxyglycerols for the protection of the blood-forming tissues against irradiation damage is also suggested.

[In a letter published in the same issue of *Nature* (p. 1102) Edlund gives a preliminary report on experiments carried out independently at the University of Uppsala in which batyl alcohol, one of the alkoxyglycerols present in bone marrow, was shown to have a protective effect on mice exposed to total body *x*-irradiation.]

E. Stanley Lee

1104. **Necrosis of the Brain following Roentgen Irradiation**

G. S. DUGGER, J. G. STRATFORD, and J. BOUCHARD. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 953–960, Dec., 1954. 7 figs., 7 refs.

1105. **Tissue Distribution of Injected Radioactive Colloidal Chromic Phosphate ($CrP^{32}O_4$)**

J. B. MCCORMICK, G. MILLES, B. JAFFE, and L. SEED. *Archives of Pathology* [*Arch. Path. (Chicago)*] **58**, 187–201, Sept., 1954. 9 figs., 24 refs.

Working at the U.S. Public Health Hospital, Chicago, the authors have investigated the possibility of using radioactive colloidal chromic phosphate ($Cr^{32}PO_4$) for the local treatment of tumours. The advantages of this substance over radioactive gold are the ease of handling, since no gamma rays are emitted, and its longer half-life (14·3 days). For this study it was prepared as a colloidal suspension in 2% pectin solution, two different particle sizes being tested, the first solution containing colloid particles of an average diameter of 0·2 μ, and the other particles ranging in size from 2 μ to 4 μ. Each 10 mg. of chemical chromic phosphate possessed 1 mc. of radioactivity.

In the first experiment an intravenous injection of 50 μc. of $Cr^{32}PO_4$ was given into the marginal ear vein of 12 mature rabbits, the animals were killed at weekly intervals, and the organs, including the lymph nodes, dissolved in 2N sodium hydroxide. One-ml. aliquots were then dried under infra-red light, and the amount of radioactivity determined by Geiger counter. It was found that almost all the dose was localized and held by the liver and spleen. To test the tolerance of these organs doses up to 250 μc. were given intravenously to rats; no gross or histological irradiation changes were found in the liver or spleen on examination at intervals up to 77 days.

In the second experiment subcutaneous injections were given into the centre of the rabbit's ear in doses varying from 100 to 400 μc. The largest dose caused a local reaction which progressed to a punched-out hole in the ear. Post-mortem examination of the animals at periods up to 85 days showed that under 2% of the radioactivity reached the adjacent lymph nodes, and none was detected in the liver or spleen. In a third study intramuscular injection of 100 to 200 μc. into the pectoral region of the rat was followed by a reaction proportional to the dose given and to the duration of exposure. After the 25th day local necrosis was the rule, at which time 7% of the total radioactivity was present in the axillary lymph nodes and 4·4% in the liver and spleen.

Finally, doses of 100 to 200 μc. were injected into one testicle of 6 rats, and produced anatomical changes proportional to the dose received; the opposite testicle was never affected. A maximum radioactivity of 5% of the given dose was found in the para-aortic, presacral, and ipsilateral iliac lymph nodes at 39 days, and up to 4·4% was detected in the liver and spleen. Intratesticular injections of the solutions of different particle size described above showed that there was increased migration to the liver and spleen of the smaller particles, and this became even more marked when they were suspended in saline instead of pectin solution.

The authors conclude from these results that there is effective localization of the larger particles of radioactive colloidal chromic phosphatase solution and that the main factors influencing migration of the isotope from the site of injection are particle size and, to a lesser extent, the nature of the suspending vehicle. The possibility of the clinical application of the method for the local treatment of neoplasms is discussed and its promise pointed out.

A. M. Jelliffe

1106. **Use of Radioactive Chromic Phosphate in Pleural Effusions**

M. L. JACOBS. *California Medicine* [*Calif. Med.*] **81**, 268–271, Oct., 1954. 2 figs., 10 refs.

Colloidal radioactive chromic phosphate ($Cr^{32}PO_4$) can be used in the same way as radioactive gold for control of the often distressing pleural effusions and ascites associated with malignant growths. Since its half-life is 14·3 days (compared with 2·69 days for gold) and the radiation consists entirely of beta rays (gold has also a gamma fraction), the dosage can be lower, handling is safer, and problems of protection are simpler.

In a series of 25 cases of pleural effusion and 12 of ascites treated by the author at the City of Hope Medical Center, Duarte, California, the doses employed ranged from 6 to 9 mc. for the pleural cases and from 9 to 12 mc. for the cases of ascites (comparable doses of gold would have been 25 to 200 mc.). The maximum energy of the particles is 1·7 meV (average 0·6 meV), and the average penetration in tissue is 2 mm., with a maximum of 7 mm., in contrast to 3·8 mm. achieved with gold. The isotope is prepared in a saline solution containing 1·0 mc. per ml.; this also contains 3·5 mg. of $CrPO_4$, which is biochemically inert and non-toxic, though its biological fate is not yet fully known. No undesirable sequelae were observed after doses up to 16 mc. The technique of injection is simple; after removal of as much fluid as possible, the isotope solution is injected through a

syringe, care being taken afterwards to isolate all objects contaminated with the radioactive substance. Of the 25 cases of pleural effusion associated with primary or secondary tumour, relief was obtained in 18 cases for periods of 1 to 15 months. Of the 12 ascitic cases, 9 were successfully controlled for 1 to 10 months. It is stated that these results compare favourably with those achieved with radioactive gold. *J. Walter*

RADIODIAGNOSIS

1107. Venographic Clues to Localization of Intracranial Masses

P. A. RIEMENSCHNEIDER and A. ECKER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 740–753, Nov., 1954. 34 figs., 5 refs.

The limitations of cerebral angiography in the diagnosis of tumours of the midbrain and the basal ganglia, which are due to the paucity of readily identifiable arteries in these regions, are discussed. The authors then show how distortion of the normal anatomy of the cerebral deep venous system may be utilized in the location of deep-seated tumours, reference being made to the work of Moniz and of Krayenbühl and Richter.

The normal anatomy of the deep venous system is described, the focal point of which is located at the foramen of Monro, where the thalamostriate vein and the vein of the septum pellucidum unite to form the " venous angle ", continuing as the internal cerebral vein. A further anatomical feature is the pineal gland, which lies 7 mm. anterior to the lowest point of the vein of Galen, which itself lies in the midline and may be displaced laterally by posteriorly placed supratentorial masses. The displacement and distortion of this venous system by suprasellar tumours with parasellar extensions, frontopolar tumours, and those sited in the anterior basal ganglia, the posterior part of the corpus callosum, and the cerebello-pontine angle are described and illustrated by diagrams and reproductions of radiographs. Mention is also made of the venographic changes seen in patients with parasagittal tumours, tumours in the temporal lobe, and subdural haematomata.

Describing their own technique the authors advocate the use of manual changing of cassettes, allowing 4 to 6 seconds between the arterial and venous phases, with stereoscopy, rather than a roll-film device.

[This is an excellent and most valuable paper.]

W. B. D. Maile

1108. Angiocardiography by the Subclavian Route. (L'angiocardiographie par voie sous-claviculaire)

R. AUBANIAC, P. VIALLET, L. SENDRA, P. COMBE, and L. CHEVROT. *Presse médicale* [*Presse méd.*] **62**, 1308–1311, Sept. 29, 1954. 15 figs., 7 refs.

The authors first criticize in some detail the methods of angiocardiography in current use. Thus injection of the contrast medium into a peripheral vein may be difficult owing to lack of a suitable vein, and it may be even more difficult to repeat the examination. The results obtained are often good, but medium is diluted by the peripheral blood during its passage to the heart, with the result that the contrast shadow in the heart and great vessels is diminished in density; moreover, the diluted medium takes some time to pass through the right heart, so that in later films the shadow of the right side of the heart is superimposed on that of the left. The method of cardiac catheterization nearly always produces good density, and the shadows of the two sides of the heart are not often superimposed on each other. However, anaesthesia is more frequently required, and the method is somewhat difficult and sometimes dangerous. Angiocardiography by direct percutaneous intracardiac injection gives the clearest picture of all, but this method is not without considerable danger which makes its use hardly justifiable.

The authors then go on to describe the technique of angiocardiography by percutaneous injection into the right subclavian vein, providing a number of illustrations of the resulting angiocardiogram. They claim for this method the following advantages. (1) It is simple and does not require general anaesthesia. (2) It is theoretically practicable at any age, though difficult during the neonatal period. (3) The examination can be repeated as often as necessary; repuncture has been performed after an interval of 8 days without any evidence of scarring being encountered. (4) There is no hazard to the vein. (5) It is possible without difficulty to use a very large needle and inject the medium rapidly, thus obtaining an excellent contrast embolus. (6) For the same reason distinction between the left and right sides of the heart is good.

The main disadvantages are that the technique of puncture of the subclavian vein is not widely known, and that there is a possibility of injection of contrast medium into the mediastinum; however, they discount the danger from such an accident, and from personal experience report that the medium causes no pain and is absorbed within a few hours. On the whole, therefore, they conclude that their method offers all the advantages of other techniques and has few of their disadvantages, and they recommend it as the method of choice.

G. H. du Boulay

1109. The Contribution of Cinedensigraphy to the Diagnosis of Cancer of the Lung. (La contribution de la cinédensigraphie au diagnostic du cancer du poumon)

R. KOURILSKY and M. MARCHAL. *Presse médicale* [*Presse méd.*] **62**, 1296–1298, Sept. 29, 1954. 6 figs., 1 ref.

The value of cinedensigraphy (Marchal, *Presse méd.*, 1953, **61**, 1734; *Abstracts of World Medicine*, 1954, **15**, 541) in the investigation of suspected cases of bronchial carcinoma when all other methods have failed to give a definite diagnosis is illustrated in a series of 50 cases reported from the Hôpital Saint-Antoine, Paris. In 21 the suspected diagnosis was either confirmed or excluded by standard methods, but in the remaining 29 a firm diagnosis was impossible until cinedensigraphy was performed. By this method, which is a modification of electrokymography, a photographic record is obtained of the vascular pulsation in the different parts of the lung

parenchyma. In 18 of the 29 cases the complete or partial suppression of pulsation in the cinedensigram from the affected lung provided evidence in favour of carcinoma, whereas in the remaining cases pulsation persisted, suggesting that no carcinoma was present. The positive diagnosis was confirmed at subsequent operation in all but 2 cases of long-standing broncho-pulmonary inflammatory disease; it was noted that in these 2 cases pulsation was not completely suppressed and that the abnormality was limited to the affected lobe, whereas when carcinoma is present pulsation is usually reduced in all the lobes on the affected side. Among those cases with no cinedensigraphic evidence of carcinoma the condition was subsequently proved to be non-malignant in all but 2—one of Hodgkin's disease and one of adenomatosis.

It is concluded that the diminution of arterial pulsation in the lung as demonstrated by cinedensigraphy is due in the majority of cases to cancer, the degree of change being proportional to the degree of malignancy of the tumour. *G. H. du Boulay*

1110. **The Roentgen Aspects of Five Hundred Cases of Pulmonary Coccidioidomycosis**
J. W. BIRSNER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 556–573, Oct., 1954. 37 figs., 13 refs.

Coccidioidomycosis is a very rare disease in Great Britain, but in the U.S.A. the author estimates that there are between 25,000 and 35,000 new cases yearly. The disease is found principally in endemic areas in Arizona and New Mexico, but is most prevalent in the San Joaquin valley in southern California. In this paper the author discusses the radiological appearances of the disease as found on examination of 500 proved cases seen at San Joaquin Hospital, Bakersfield, California. The cases are divided into three groups according to age, the numbers in the three age groups 0–13, 14–60, and 60+ being 124, 352, and 24 respectively.

The site of the disease may be tracheobronchial or pulmonary, but general dissemination is not uncommon. The *x*-ray appearances are extremely varied and comprise areas of infiltration, enlarged hilar nodes, solitary or multiple round lesions, cavitation, pleural effusions, fibrosis, and calcification. The disease closely resembles tuberculosis and may mask the presence of the latter; both conditions were present in 24 of the patients. Hilar-node enlargement may be a striking feature, producing an appearance very similar to that of reticulo-endotheliosis, while most of the possible appearances of a bronchial carcinoma can be simulated by coccidioidomycosis. Erythema nodosum was an early feature in 8 of the author's cases.

There are no specific radiological features of the disease, and confirmation of the diagnosis depends upon a positive complement-fixation test or isolation of the aetiological agent (*Coccidioides immitis*). The condition is serious, deaths numbering 57 in the present series, although only 7 of these occurred among the 124 patients in the 0–13 age group. While there is no specific treatment, it is important to confirm every case to avoid the risk of neglecting some condition, such as an early carcinoma, which may be more amenable to treatment. In endemic areas the diagnosis of pulmonary tuberculosis and other chest lesions is rendered more difficult because of the high incidence of coccidioidomycosis in the population. *D. E. Fletcher*

1111. **The Administration of Barium Orally in Acute Obstruction; Advantages and Risks.** [In English]
J. FRIMANN-DAHL. *Acta radiologica* [*Acta radiol. (Stockh.)*] **42**, 285–295, Oct., 1954. 7 figs., 7 refs.

As a result of his extensive experience in radiology of the acute abdomen, the author contests the generally held view that the oral administration of barium suspensions is contraindicated in the presence of any form of acute obstruction. He agrees that this view is valid for obstruction of the large intestine, where absorption of water causes inspissation of the barium and increases the degree of obstruction. In small-bowel obstruction, however, barium becomes more and more diluted as it approaches the site of the stenosis, so that the degree of obstruction will not be increased. Out of 445 such cases examined after the oral administration of barium at Ullevål Hospital, Oslo, between 1942 and 1952 a correct diagnosis was made in all but 24 (5%), while the mortality has gradually diminished.

If a satisfactory diagnosis cannot be made from the clinical examination and study of routine plain films, and if an obstruction in the large intestine cannot be excluded, a barium enema should be administered first; if the diagnosis is still obscure, examination of the small intestine may then be carried out. For this purpose not more than 20 ml. of barium suspension (2 parts barium sulphate, 3 parts water) is given by mouth. The patient then lies on his right side to ensure emptying of the stomach, and the progress of the barium through the small bowel is followed on serial films until the site of obstruction is reached. In the author's experience obstruction of the small intestine, usually due to adhesions or bands, or to kinking, twisting, or incarceration of the bowel, is complete in approximately 50% of cases, and requires operation. In the majority of the remaining cases, where obstruction is incomplete, the condition usually resolves without operation.

Oral barium is of most value in the diagnosis of early cases of obstruction, and its use is contraindicated when the condition is advanced—as shown in the plain film by the presence of fluid or gas in the peritoneal cavity. It is also of value in the differentiation of other conditions which may at some stage simulate mechanical obstruction, such as acute appendicitis, salpingitis, pancreatitis, cholecystitis, and regional enteritis, and in the post-operative investigation of suspected ileus.

Attention is drawn to the risk of undue prolongation of the observation period before operation. It is, however, usually possible to reach a diagnosis within 8 to 12 hours, and the author considers the risk to be more than offset by the increased precision of diagnosis. There is also a risk that in cases of unsuspected perforated peptic ulcer simulating obstruction barium may enter the peritoneal cavity; in 5 such cases in the author's series this was easily recognized and did not appear to compli-

cate the subsequent operation. A further disadvantage is the possible retention of barium in the colon during the postoperative period, but this does not usually cause any trouble except occasionally in patients who have previously had a barium enema for examination of a colonic lesion. *G. Ansell*

1112. **Simultaneous Arteriography of the Abdominal Aorta and of the Arteries of the Lower Extremities**
F. E. CHRISTMANN and D. GRINFELD. *Angiology* [*Angiology*] **5**, 339–352, Aug., 1954. 6 figs.

A method of arteriography of the abdominal aorta and arteries of the lower limbs is described in which one injection of contrast medium is made into the abdominal aorta under local analgesia. [No details are given of the method of injection or of the amount of radio-opaque substance used, the authors confining themselves mainly to the radiographic technique.]

An angiocardiograph is used, and films in 4 positions are obtained by moving the patient in relation to the angiocardiograph in the intervals between films. The first radiograph, of the abdomen, is taken 4 to 5 seconds from the start of the injection, subsequent radiographs being taken at 2- to 3-second intervals. Owing to the variation in the rate of flow of the medium—due to various causes—the fourth radiograph may be negative or may even show the dye in the veins.

The authors briefly describe a series of 8 cases in which this technique was used; in 2 cases there were complications—myocardial infarction in one and lower nephron nephrosis in the other. *L. G. Blair*

1113. **Abdominal Aortography for the Roentgen Demonstration of the Liver and Spleen**
L. G. RIGLER and P. C. OLFELT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 586–596, Oct., 1954. 11 figs., 20 refs.

Until recently radiology has contributed little to the investigation of hepatic or splenic pathological conditions. The outline of both organs may be shown to a limited extent, or to a greater extent if a pneumoperitoneum is performed, but nothing can be shown of the internal structure unless calcified lesions are present, or some form of contrast material can be introduced. "Thorotrast" is one such contrast medium, but it has obvious drawbacks and no safe alternative has yet been found. The problem may be tackled by means of angiography, however, and the authors, working at the University of Minnesota, have evolved an angiographic technique which employs abdominal aortography to demonstrate the organs. The aorta is punctured from the back just below the 11th rib and above the 11th dorsal vertebra, and 40 ml. of 70% "urokon" injected. Films are taken every second for 18 seconds.

In addition to the conventional aortogram, both the hepatic and splenic arteries fill well. The large quantity of dye used and the high site of injection result in satisfactory filling of the portal system and opacification of the liver and spleen, as well as of the kidneys. The degree of opacity of the liver is not great, but is adequate to demonstrate the presence of space-occupying lesions. It is not possible to determine with any certainty whether such lesions are benign or malignant, since many hepatic tumours are necrotic and therefore no circulation in the tumour can be visualized. The authors stress the value of the method for the location of a mass within the liver, and also in demonstrating single metastases which it may be possible to remove. They have also investigated cases of hepatic cirrhosis, in which they found that a marked delay and diminution of opacification occur. *D. E. Fletcher*

1114. **Intravenous Cholangiography**
F. GLENN, J. EVANS, M. HILL, and J. MCCLENAHAN. *Annals of Surgery* [*Ann. Surg.*] **140**, 600–614, Oct., 1954. 14 figs., 14 refs.

The authors report, from New York Hospital–Cornell Medical Center, their experience in the performance of cholangiography 88 times in 80 patients with a promising new contrast agent, "cholografin", which is a 20% solution of the di-sodium salt of triiodobenzoic acid and is administered intravenously. It is prudent to carry out a preliminary test for hypersensitivity with 1 ml. In practice a single dose of 20 ml. usually suffices to demonstrate the biliary ducts in a thin patient, but double this dose does not seem to produce more side-effects and gives radiographs of better diagnostic quality. The substance should not be given to patients with hyperthyroidism or known idiosyncracy to iodine, and there is some risk, at least in theory, in giving it to patients with chronic progressive liver disease. The method of administration is described in great detail. It was found that toxic reactions could be kept to a minimum if the agent was injected slowly over a period of 10 minutes. The injection should be temporarily interrupted if there is any complaint of nausea or abdominal pain. In only 2 cases (2·5%) did fairly severe reactions occur; these were characterized by vomiting, dyspnoea, and a boring epigastric pain lasting approximately 30 minutes. Milder reactions were observed in 31 patients (38·8%), who complained chiefly of nausea and flushing beginning when about half the dose had been given, but these were gradually relieved by deep breathing and slowing of the rate of injection.

With the patient prone and the right side slightly elevated radiographs are taken in the postero-anterior projection at 15 and 20 minutes after the injection and developed at once so that further radiographs or tomograms may be obtained if necessary. The common bile-duct is usually visible from 10 to 60 minutes after injection and then gradually fades. The normal gall-bladder begins to opacify in about 50 minutes, increasing in density for about 2 hours. After the gall-bladder has been demonstrated a fatty meal may be given, this being followed 30 minutes later by a further film. The length of time the biliary tract is visualized can be prolonged to some extent by inducing spasm of the sphincter of Oddi with morphine or tincture of opium before injecting the contrast agent.

In the entire series of 80 patients the common bile-duct was demonstrated in 53 cases (66·2%), but was never

visualized in the presence of jaundice. Cholecystectomy had been previously performed in 30 of the cases, and among these the common duct was shown in 24 (80%); jaundice accounted for the lack of visualization in 4 cases and in one other case there was laboratory evidence of liver damage. The authors stress in conclusion that this method of investigation does not, and is not intended to, take the place of oral cholecystography, which in addition to providing delineation of calculi gives valuable information as to the function of the gall-bladder.

L. G. Blair

1115. **Practical Procedure for the Detection of Biliary Dyskinesia by Cholecystographic Intubation.** (Procédé pratique de la détection des dyskinésies biliaires par le tubage cholécystographique)

R. IMBERT. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 889–906, Sept.–Oct., 1954. 4 figs., 16 refs.

The author describes his technique for examining cases of biliary dyskinesia by simultaneous cholecystography and duodenal intubation. Cholecystography is carried out with " telepaque " (iopanoic acid) given by mouth the evening before, or with " biligrafin " injected intravenously 2 hours before the test; telepaque has given the more satisfactory results. A preliminary film is taken to confirm that the contrast medium is satisfactorily concentrated in the gall-bladder. The duodenal tube is then introduced under screening control. When bile appears 20 ml. of olive oil is injected through the tube. Films are taken at 5, 10, and 15 minutes, but if the sphincter of Oddi remains closed at 15 minutes 10 ml. of 1% procaine is introduced and a film taken at 17 minutes. If no bile is obtained the test is repeated using amyl nitrite.

The author details the findings in a normal subject, in cases of pure cystic-duct obstruction or pure spasm of the sphincter of Oddi, in cases in which these two conditions are combined, and in stasis of the gall-bladder. It is claimed that by this test it is possible to differentiate these conditions. *John H. L. Conway-Hughes*

1116. **The Diagnosis of Hydronephrosis by Percutaneous Renal Puncture**

H. S. WEENS and T. J. FLORENCE. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 589–595, Oct., 1954. 4 figs., 5 refs.

The authors advocate direct percutaneous puncture of the kidney and the injection of a contrast medium into the pelvis or calyces in cases of renal hydronephrosis in which satisfactory results are not obtainable by the conventional means of excretory or retrograde urography. With the patient prone a local analgesic is injected over the renal region (or over a palpable mass, if present), which may be supplemented by blockade of the lower intercostal nerves. A 5-inch (12·7-cm.), 18-gauge needle attached to a 5-ml. or 10-ml. syringe is then inserted in the direction of the mass if one is palpable, or under radiographic control if the kidney cannot be felt, and an attempt made to withdraw urine. If this is successful, 20 to 30 ml. of 35% diodone is injected; if not, 10 to 20 ml. is injected at the estimated depth in the hope of delineating renal structures. Details of 4 cases in which this procedure was carried out are given; there were no complications.

[This would appear to be a potentially dangerous investigation, especially the introduction of contrast medium in the absence of any evidence that the renal pelvis has been entered.] *W. B. D. Maile*

1117. **Roentgen Changes Observed in Generalized Scleroderma. Report of Sixty-three Cases**

J. A. BOYD, S. I. PATRICK, and R. J. REEVES. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 248–258, Aug., 1954. 17 figs., 9 refs.

The radiological findings in 63 cases of scleroderma seen over a recent 20-year period at Duke Hospital, Durham, North Carolina are described. Women outnumbered men by slightly more than 2 to 1, and the majority of the patients (67%) were between 31 and 50 years of age. In 60 cases there was significant clinical evidence of soft-tissue or vascular changes in the hands.

Chest radiographs were taken in 54 cases and in 24 of these an abnormality was observed in the lungs, usually an infiltrative process in the central portion of both bases, which tended to clear partially and then to recur, with increased distribution. In 2 cases large pneumonoceles were seen, with subsequent development of a pneumothorax. In 23 out of 29 cases in which the gastrointestinal tract was examined the oesophagus was abnormal; moreover, in those cases in which the stomach and small bowel were examined as well abnormality of these organs was an associated finding. The changes in the oesophagus varied widely; in some cases there was narrowing in the region of the cardia, with dilatation, loss of peristaltic activity above, and retention of barium; in others, a generally narrow oesophagus with rigid walls was observed. The stomach appeared dilated and there was delay in emptying. In the small bowel abnormality of segmental width and neuromuscular disturbances were noted. The phalanges of the hand were examined in 31 cases, and in 18 varying degrees of sclerodactyly were present. This always originated as resorption of the terminal phalanx, progressing proximally. In 27 out of 31 cases there was definite abnormality of the soft tissues of the hands, which consisted in swelling or atrophy of the part; in some cases calcium deposits were present, and linear streaks of decreased density were a characteristic early finding. As regards the joints, changes similar to those seen in rheumatoid arthritis were found in 17 out of 31 cases. There was cardiac enlargement, thought to be due to the disease process, in 22 out of 54 cases, while enlargement of the liver and spleen was found in 13 out of 24 cases. Evidence of marked sinusitis was observed in all 6 cases in which the maxillary sinus was examined.

John H. L. Conway Hughes

1118. **Treatment of Hemangioma of the Skin in Infancy and Childhood by Roentgen Irradiation and Radium. (A Report of 323 Cases)**

A. ABDULKERIM, J. A. BOYD, and R. J. REEVES. *Pediatrics* [*Pediatrics*] **14**, 523–527, Nov., 1954. 8 refs.

History of Medicine

1119. **Molière, Boileau, La Fontaine, and the Circulation of the Blood.** (Molière, Boileau, La Fontaine et la circulation du sang)
L. Chauvois. *Presse médicale* [*Presse méd.*] **62**, 1219–1220, Sept. 11, 1954. 1 fig., 4 refs.

More than a century elapsed after the publication of Harvey's *De motu cordis* in 1628 before his doctrine of the circulation of the blood finally ousted the concepts of Galenic physiology, and the events described in this article show that bitter controversy was raging in France as late as the period 1671–90.

Harvey had found some support from René Descartes and other writers, but antagonism to the new theory was widespread, and centred on the Faculté de Médecine de Paris, which for 20 years after the death of Descartes succeeded in suppressing it. The decisive move in breaking this opposition came from King Louis XIV himself who, influenced by his more progressive medical advisers, re-established in 1671 the chair of anatomy at the Jardin du Roy and appointed Pierre Dionis to give public lectures in accordance with the new ideas. The Faculté, jealous of its teaching privileges as well as conservative in its theories, attempted to fight this appointment, but was overridden by the king, who came in person to parliament to issue his decrees.

The combined effect of this public uproar and of the popular lectures by Dionis is shown in quotations from three great authors of the period. Molière and Boileau, eager to amuse the Court and society, were quick to seize upon the circulation theory as material for satirizing the established medical authorities, while La Fontaine, in a little-known poem entitled *Quinquina*, dated 1682, gives a lyrical description of the circulatory system. By their wider contact with the public, these non-medical writers probably contributed even more to the final acceptance of Harvey's discoveries than the lectures of Dionis. *F. M. Sutherland*

1120. **How Medicine Became Anatomical**
C. Singer. *British Medical Journal* [*Brit. med. J.*] **2**, 1499–1503, Dec. 25, 1954. 4 figs.

The author, in his Lloyd Roberts Lecture to the Medical Society of London in September, 1954, traced the development of anatomy to its present status "as the basic positive discipline" of the art of medicine. Anatomy has not always been regarded as the foundation of the art of medicine; modern acceptance of this idea is due to the reformers of the 16th century, especially to Vesalius. Before the time of Vesalius there were many distinguished physicians who laid no stress upon anatomy, while since his time there have been others of like mind; even today certain branches of medicine are developing without any clear anatomical background. In early times the fear of being disrespectful to the dead was a strong deterrent to dissection. The Hippocratic physicians were keen clinical observers; yet they made no deep study of anatomy, and it was not until about 300 B.C. that systematic dissection was first practised in the great medical school of Alexandria. When Roman power succeeded Greek there was a return of the former attitude to the dead, and even in Alexandria anatomy was no longer taught at the end of the second century A.D. The anatomy of Galen was based upon animal dissection, and in any case the ancient anatomy, devoid of graphic figures or technical vocabulary, could not hope to survive.

The history of anatomy for the next thirteen centuries is almost a blank. Then the study was revived by the leading artists of the Renaissance. Within half a century four factors determined the course of anatomical development. "First was the rise of the science of perspective," of which Leonardo was the leading exponent. "Second was the intimately related development of skill in exact representational drawing. Third was the publication of the ancient anatomical texts from which the new anatomy could take its start. Fourth was the perfection of the art of book illustration, so that the anatomist could at last present his findings graphically and acceptably to a wide audience." This last was almost personified in one man, Vesalius. He had the judgment and power to correlate a wide practical experience with the services of artists trained in Leonardian perspective. Anatomy became modern at one bound, so far as the printed book was concerned. Much has been learned since his time, but in method we are not very far from him. Admittedly both Vesalius and Leonardo sometimes followed tradition too faithfully, and in some respects the work of Eustachius was more accurate. Nevertheless they laid the foundations. The vast folio of Vesalius was not for the ordinary student's desk, but it was followed by the textbook of the Dane, Caspar Bartholin (1611), and, in due course, by a succession of textbooks on anatomy and physiology down to our own day.

[This clear account of one of the most important trends in medicine, so ably handled by the acknowledged authority in Britain on medical history, deserves the close attention of every medical teacher and practitioner.] *Douglas Guthrie*

1121. **Physicians and Surgeons in Bologna and Ravenna in the Time of Dante.** (Medici e chirurghi in Bologna e in Ravenna ai tempi di Dante)
G. Forni. *Giornale di clinica medica* [*G. Clin. med.*] **35**, 1077–1094, Sept., 1954.

1122. **Medical and Surgical Treatment at St. Thomas's Hospital in the Times of Elizabeth I and James I (1558–1625)**
E. M. McInnes. *St. Thomas's Hospital Gazette* [*St Thom. Hosp. Gaz.*] **52**, 177–182, Oct., 1954.